STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 161026

TO: Rei-Tsang Shiao **Location: 5a10 / 5c18** **Thursday, August 04, 2005** **Art Unit: 1626** **Phone: 571-272-0707** **Serial Number: 10 / 743365**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Remsen 1a51** **Phone: 571-272-2504** **jan.delaval@uspto.gov**

Search Notes

FOR OFFICIAL USE ONLY 161026 ACCESS DB # _____
PLEASE PRINT CLEARLY

Jain Related to search

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Robert (Rob) Shin Examiner #: 79521 Date: 8/1/05
Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/743365
Location (Bldg/Room#): KP7 (Mailbox #): 5A10/5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Process for the manufacture
Inventors (please provide full names): Muller et al

Earliest Priority Date: _____

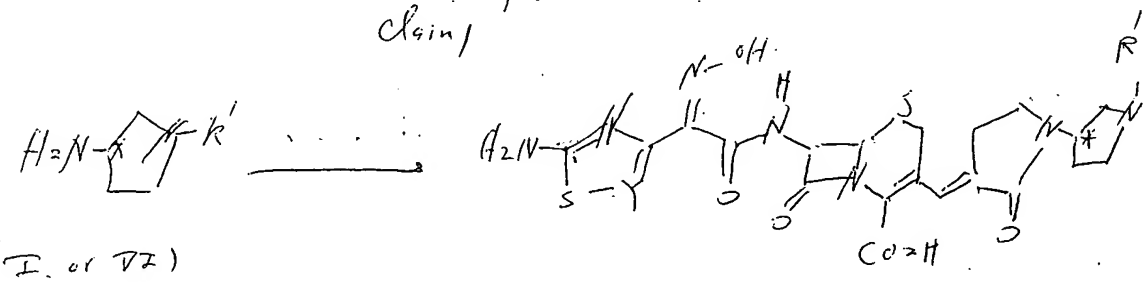
Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

2. Search a process by making cpd A. by

(see scheme 1, page 8)

claim 1



(I. or II)

Y is CH, or N

****

STAFF USE ONLY

Searcher: Jain
Searcher Phone #: 32604
Searcher Location: _____
Date Searcher Picked Up: 8/4/05
Date Completed: 8/4/06
Searcher Prep & Review Time: 15
Online Time: ~20

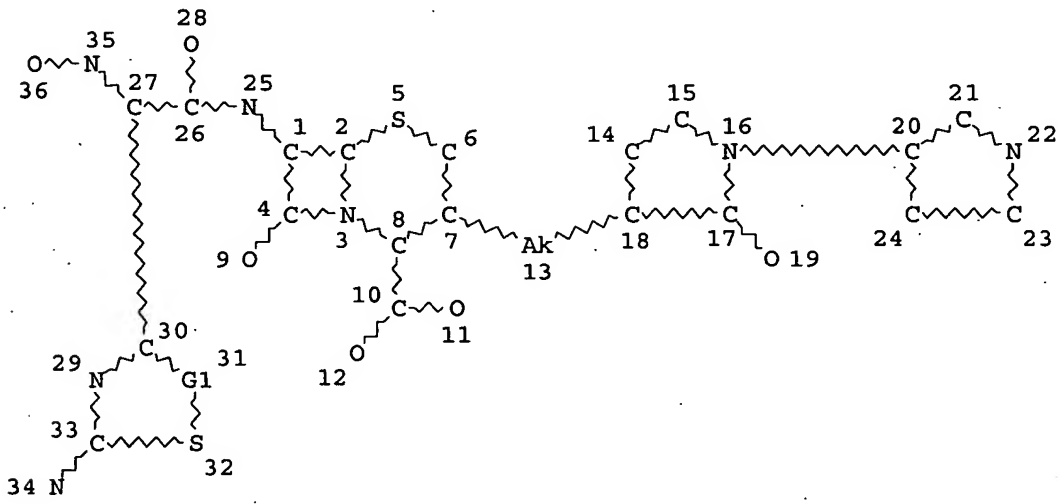
Type of Search

_____ NA Sequence (#)
_____ AA Sequence (#)
✓ Structure (#)
_____ Bibliographic
_____ Litigation
_____ Fulltext
_____ Other

Vendors and cost where applicable

✓ STN _____ Dialog
_____ Questel/Orbit _____ Lexis/Nexis
_____ Westlaw _____ WWW/Internet
___ In-house sequence systems
___ Commercial ___ Oligomer ___ Score/Length
___ Interference ___ SPDI ___ Encode/Transl
_____ Other (specify)

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 12:52:28 ON 04 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    3 AUG 2005  HIGHEST RN 858181-56-3
DICTIONARY FILE UPDATES:   3 AUG 2005  HIGHEST RN 858181-56-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l8
L1              STR
```

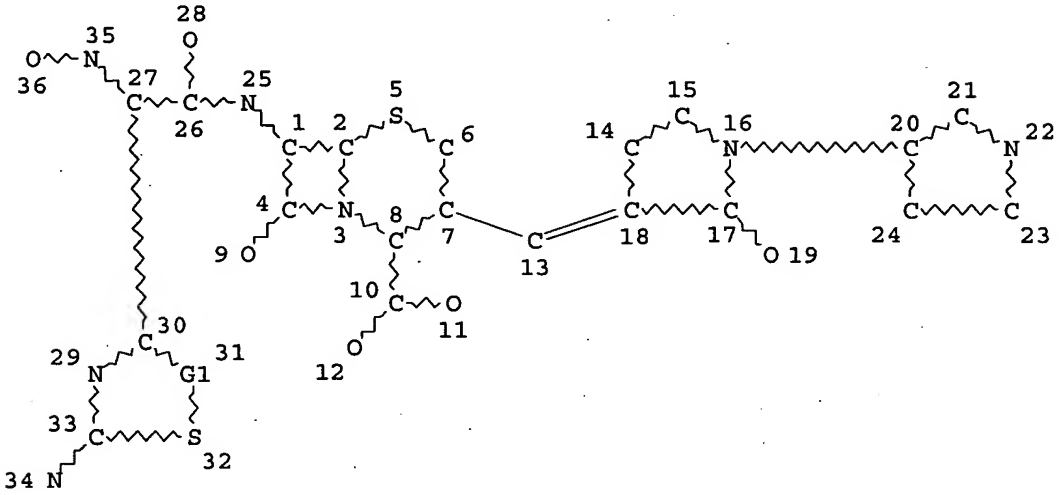



```
VAR G1=C/N
NODE ATTRIBUTES:
```

DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 36

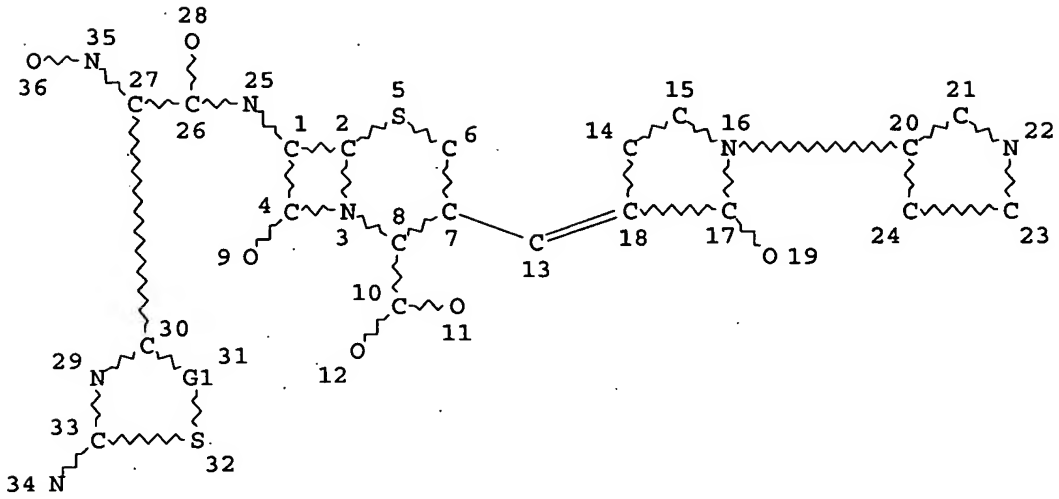
STEREO ATTRIBUTES: NONE
L3 96 SEA FILE=REGISTRY SSS FUL L1
L4 STR



VAR G1=C/N
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 11
CONNECT IS M1 RC AT 22
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE
L6 53 SEA FILE=REGISTRY SUB=L3 CSS FUL L4
L7 STR



VAR G1=C/N
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 22
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE
L8 25 SEA FILE=REGISTRY SUB=L6 CSS FUL L7

100.0% PROCESSED 53 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

=> d his

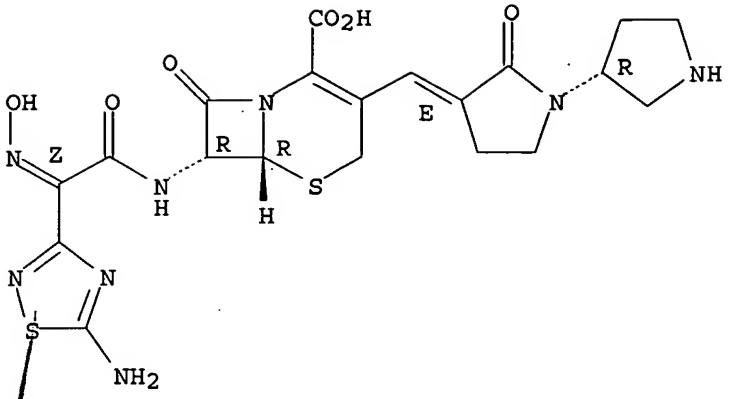
(FILE 'HOME' ENTERED AT 12:36:22 ON 04 AUG 2005)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 12:36:46 ON 04 AUG 2005
L1 STR
L2 0 S L1
L3 96 S L1 FUL
SAV L3 SHIAO743/A
L4 STR L1
L5 0 S L4 CSS SAM SUB=L3
L6 53 S L4 CSS FUL SUB=L3
SAV L6 SHIAO743A/A
L7 STR L4
L8 25 S L7 CSS FUL SUB=L6
SAV L8 SHIAO743B/A

FILE 'HCAOLD' ENTERED AT 12:42:09 ON 04 AUG 2005
L9 0 S L8

```
     FILE 'HCAPLUS' ENTERED AT 12:42:40 ON 04 AUG 2005
L10           27 S L8

     FILE 'HCAPLUS' ENTERED AT 12:43:14 ON 04 AUG 2005
L11           22 S CEFTOBIPROLE OR BAL9141 OR BAL 9141 OR RO 63 9141 OR RO 65 57
L12           29 S L10,L11
L13            1 S (US20040127703 OR US6872836 OR US20040034236#)/PN OR (US2003-
                 E MULLER M/AU
L14          899 S E3-E27
                 E MULLER MARC/AU
L15           69 S E3-E5
                 E MUELLER MARC/AU
L16           28 S E3-E6
                 E MUELLER M/AU
L17         1295 S E3-E25
                 E MEULLER M/AU
L18            1 S E5
                 E SOUKUP M/AU
L19           36 S E3,E9
                 E BASO
                 E BASILEA/PA,CS
L20           41 S E3-E17
L21            5 S L12 AND L13-L20
L22           29 S L12 OR BAL5788
L23            5 S L22 AND L13-L20
L24           15 S L22 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L25            6 S L22 (L) PREP+NT/RL
L26            5 S L24 AND L25
L27            8 S L23,L26
L28            8 S L25-L27
L29           10 S L24 NOT L28

     FILE 'USPATFULL' ENTERED AT 12:51:59 ON 04 AUG 2005
L30            5 S L8/P

     FILE 'REGISTRY' ENTERED AT 12:52:28 ON 04 AUG 2005

=> fil uspatful
FILE 'USPATFULL' ENTERED AT 12:52:39 ON 04 AUG 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Aug 2005 (20050802/PD)
FILE LAST UPDATED: 2 Aug 2005 (20050802/ED)
HIGHEST GRANTED PATENT NUMBER: US6925651
HIGHEST APPLICATION PUBLICATION NUMBER: US2005166296
CA INDEXING IS CURRENT THROUGH 2 Aug 2005 (20050802/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Aug 2005 (20050802/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
```

```
>>>  /PK, etc.                                                          <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d l30 bib abs hitstr tot

L30  ANSWER 1 OF 5  USPATFULL on STN
AN     2004:166213  USPATFULL
TI     Process for the manufacture of 3-amino-pyrrolidine derivatives
IN     Muller, Marc, Saint-Louis, FRANCE
       Soukup, Milan, Bottmingen, SWITZERLAND
PI     US 2004127703      A1   20040701
AI     US 2003-743365     A1   20031222 (10)
RLI    Division of Ser. No. US 2003-629483, filed on 29 Jul 2003, PENDING
PRAI   EP 2002-16944       20020801
DT     Utility
FS     APPLICATION
LREP   GIBBONS, DEL DEO, DOLAN, GRIFFINGER & VECCHIONE, 1 RIVERFRONT PLAZA,
       NEWARK, NJ, 07102-5497
CLMN   Number of Claims: 2
ECL    Exemplary Claim: 1
DRWN   No Drawings
LN.CNT 334
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The invention is concerned with a process for the manufacture of
       vinylpyrrolidinone-cephalosporin derivatives from 3-amino-pyrrolidine
       derivatives of the formula   ##STR1##

       wherein

       R.sup.1 signifies hydrogen or an amino protecting group;

       Z signifies hydrogen or an amino protecting group; and

       * represents a center of chirality.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT  209467-52-7P
       (process for asym. synthesis of cephalosporin amino-pyrrolidine
       derivs.)
RN   209467-52-7  USPATFULL
CN   5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
       7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-
       oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)-
       (9CI)  (CA INDEX NAME)

       Absolute stereochemistry.
       Double bond geometry as shown.
```



L30 ANSWER 2 OF 5 USPATFULL on STN
AN 2004:45242 USPATFULL
TI Process for the manufacture of 3-amino-pyrrolidine derivatives
IN Muller, Marc, Saint-Louis, FRANCE
Soukup, Milan, Bottmingen, SWITZERLAND
PI US 2004034236 A1 20040219
US 6872836 B2 20050329
AI US 2003-629483 A1 20030729 (10)
PRAI EP 2002-16944 20020801
DT Utility
FS APPLICATION
LREP GIBBONS, DEL DEO, DOLAN, GRIFFINGER & VECCHIONE, 1 RIVERFRONT PLAZA, NEWARK, NJ, 07102-5497
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 363
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is concerned with a process for the manufacture of 3-amino-pyrrolidine derivatives of the formula ##STR1##

wherein

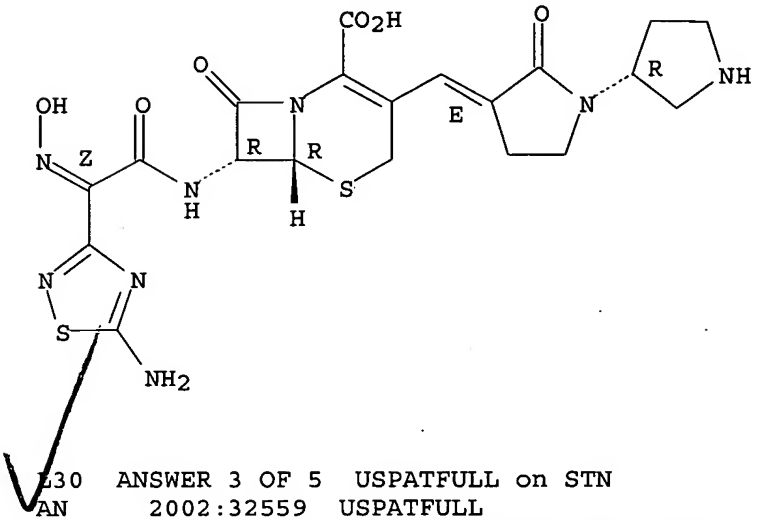
R.sup.1 signifies hydrogen or an amino protecting group;

Z signifies hydrogen or an amino protecting group; and

* represents a center of chirality. 3-Amino-pyrrolidine derivatives, especially optically active 3-amino-pyrrolidine derivatives, are intermediates for the production of agrochemicals and of pharmaceutically active substances such as, for example, of vinylpyrrolidinone-cephalosporin derivatives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **209467-52-7P**
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)
RN 209467-52-7 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)-(9CI) (CA INDEX NAME)

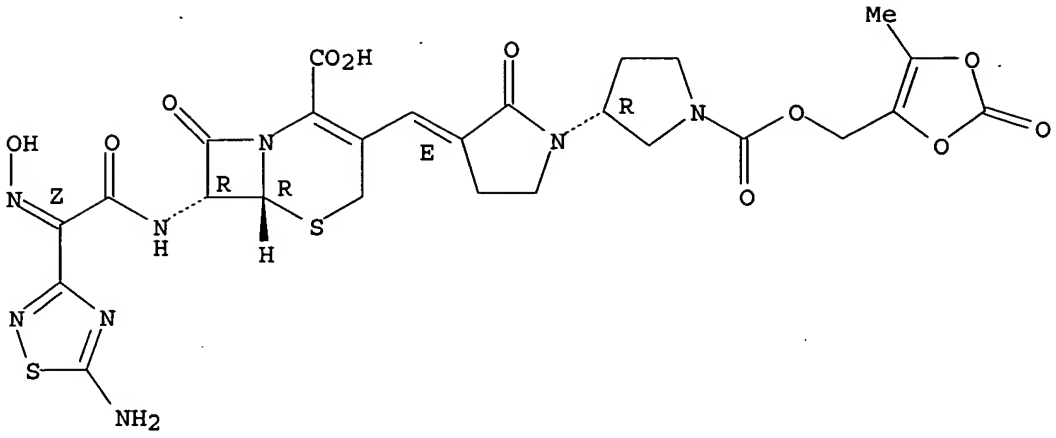
Absolute stereochemistry.
Double bond geometry as shown.



L30 ANSWER 3 OF 5 USPATFULL on STN
AN 2002:32559 USPATFULL
TI Process for the preparation of vinyl-pyrrolidinone cephalosporin derivatives
IN Hebeisen, Paul, Basle, SWITZERLAND
Hilpert, Hans, Reinach, SWITZERLAND
Humm, Roland, Riehen, SWITZERLAND
PI US 2002019381 A1 20020214
US 6504025 B2 20030107
AI US 2001-860157 A1 20010517 (9)
PRAI EP 2000-111164 20000524
DT Utility
FS APPLICATION
LREP HOFFMANN-LA ROCHE INC., PATENT LAW DEPARTMENT, 340 KINGSLAND STREET, NUTLEY, NJ, 07110
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 826
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process is provided for the preparation of vinyl-pyrrolidinone cephalosporine derivatives. Intermediates of the process are also provided.

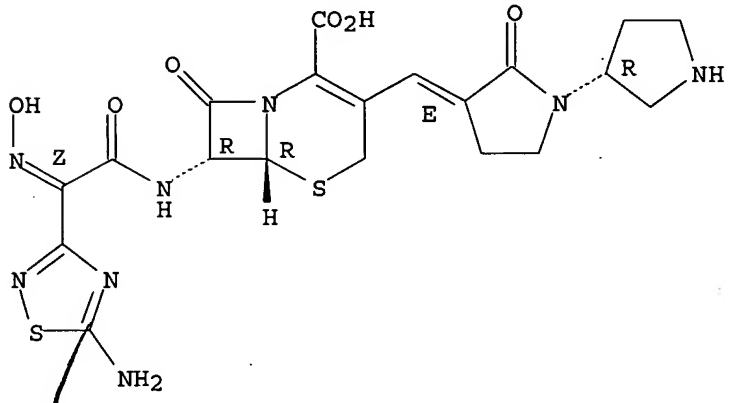
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **376653-43-9P**
(process for preparing pyrrolidinone cephalosporin derivs.)
RN 376653-43-9 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **209467-52-7P**
(process for preparing pyrrolidinone cephalosporin derivs.)
RN 209467-52-7 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L80 ANSWER 4 OF 5 USPATFULL on STN
AN 2001:71541 USPATFULL
TI Derivatives of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams
IN Hebeisen, Paul, Basel, Switzerland
Hubschwerlen, Christian, Durmenach, France
Specklin, Jean-Luc, Kembs-Schaferhof, France
PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 6232306 B1 20010515
AI US 1999-332811 19990614 (9)
RLI Continuation-in-part of Ser. No. US 1999-315715, filed on 20 May 1999
PRAI EP 1998-110888 19980615
EP 1998-117099 19980910
DT Utility
FS Granted

EXNAM Primary Examiner: Berch, Mark L.
LREP Johnston, George W., Rocha-Tramaloni, Patricia S., Ebel, Eileen M.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 495
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compounds of formula I ##STR1##

wherein

R.sup.1 is hydrogen, C.sub.1-6 -alkyl, C.sub.1-6 -alkyl substituted by fluoro, or C.sub.3-6 -cycloalkyl;

R.sup.2 is hydrogen or a substituent selected from the group consisting of --CH.sub.2 C(.dbd.CHR)--COOR, --CH.sub.2 OCOR, --CH(R)OCOR, --CH(R)OCOOR, --CH(OCOR)OCOR, --CH.sub.2 COCH.sub.2 OCOR and ##STR2##

R.sup.3 is hydrogen or a substituent selected from the group consisting of --CH.sub.2 C(.dbd.CH.sub.2)--COOR, --COOCH.sub.2 C(.dbd.CHR)--COOR, --COOCH.sub.2 OCOR, --COOCH(R)OCOR, --COOCH(R)OCOOR, --COOCH(OCOR)OCOR, --COOCH.sub.2 COCH.sub.2 OCOR, and ##STR3##

with the proviso that one of R.sup.2 and R.sup.3 is hydrogen and the other is not hydrogen,

R is hydrogen or C.sub.1-6 -alkyl;

R.sup.4 is hydrogen or hydroxy,

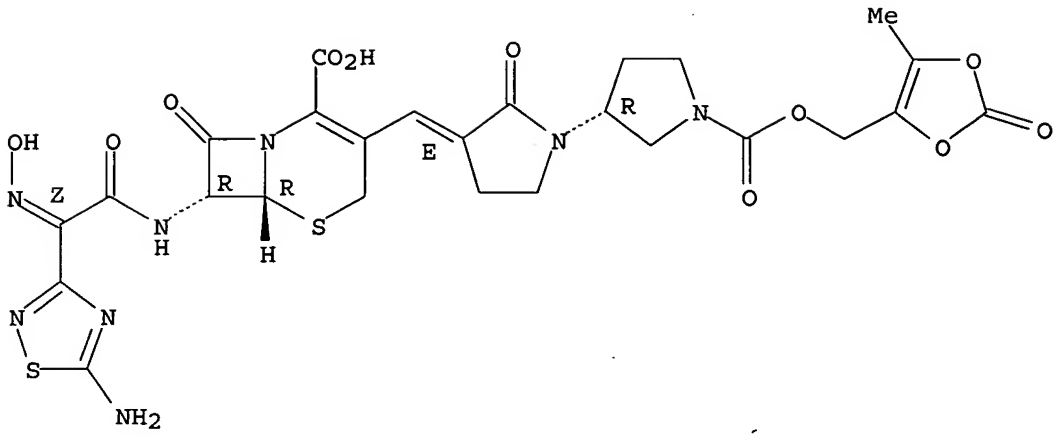
R.sup.5 is hydrogen or ω-hydroxyalkyl; and

X is CH or N,

pharmaceutically acceptable salts of the compounds and hydrates of the compounds and of their salts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **252188-71-9P 252188-72-0P 252188-73-1P**
252188-74-2P 252188-75-3P 252188-78-6P
338392-90-8P
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)
RN 252188-71-9 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

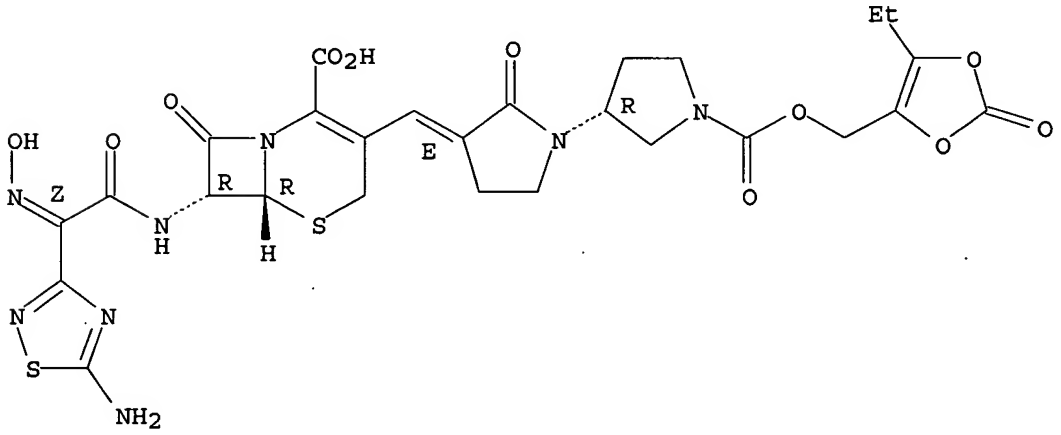
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-72-0 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-ethyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

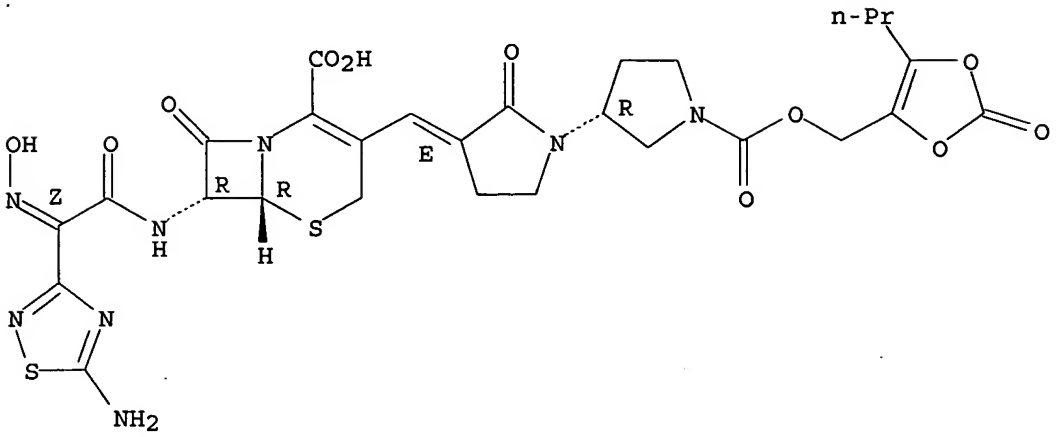


● Na

RN 252188-73-1 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo-1'-[[(2-oxo-5-propyl-1,3-dioxol-4-yl)methoxy]carbonyl][1,3'-bipyrrolidin]-3-ylidene]methyl]-, monosodium

salt, (6R,7R)- (9CI) (CA INDEX NAME)

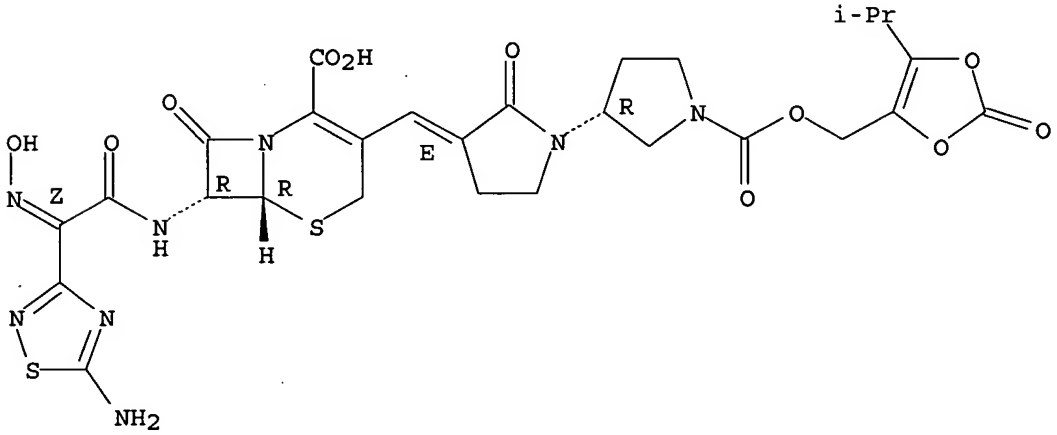
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-74-2 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[5-(1-methylethyl)-2-oxo-1,3-dioxol-4-yl]methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

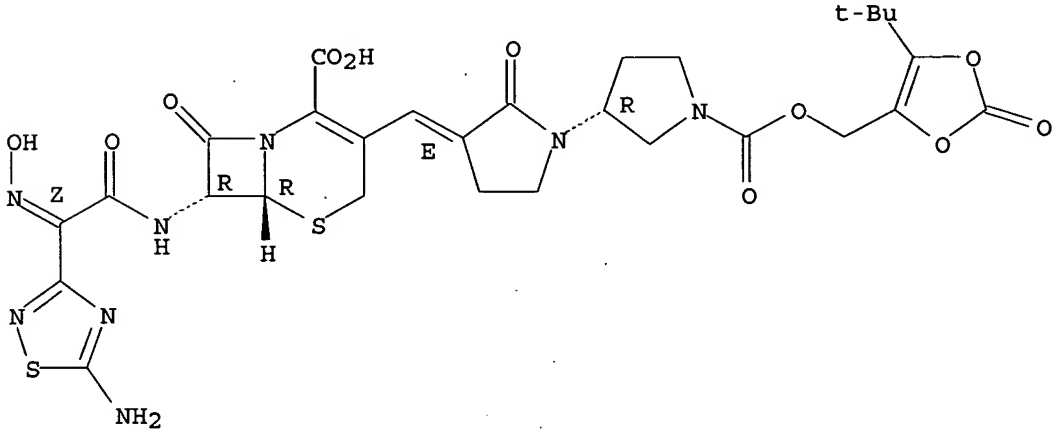


● Na

RN 252188-75-3 USPATFULL

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[5-(1,1-dimethylethyl)-2-oxo-1,3-dioxol-4-yl]methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

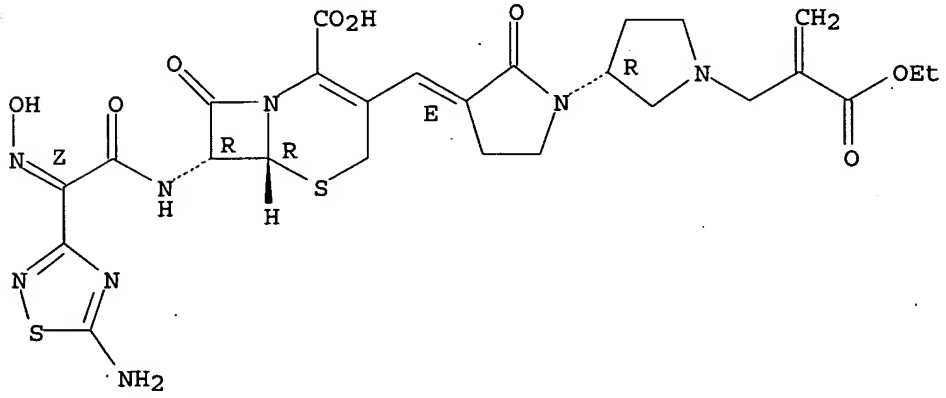
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-78-6 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[2-(ethoxycarbonyl)-2-propenyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

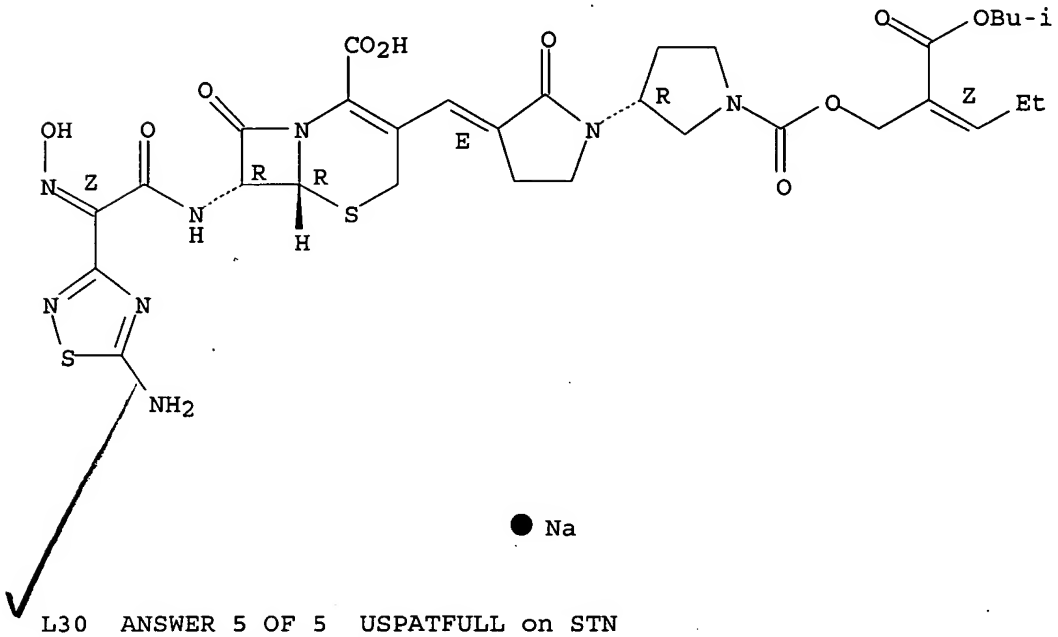
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 338392-90-8 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[(2Z)-2-[(2-methylpropoxy)carbonyl]-2-pentenyl]oxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L30 ANSWER 5 OF 5 USPATFULL on STN
AN 1999:141926 USPATFULL
TI Vinyl-pyrrolidinone cephalosporins
IN Angehrn, Peter, Bockten, Switzerland
Hebeisen, Paul, Basel, Switzerland
Heinze-Krauss, Ingrid, Schliengen, Germany, Federal Republic of
Page, Malcolm, Basel, Switzerland
Runtz, Valerie, Rixheim, France
PA Hoffman-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 5981519 19991109
AI US 1997-986549 19971208 (8)
PRAI EP 1996-120472 19961219
EP 1997-119528 19971107
DT Utility
FS Granted
EXNAM Primary Examiner: Berch, Mark L.
LREP Johnston, George W., Rocha-Tramaloni, Patricia S., Kass, Alan P.
CLMN Number of Claims: 65
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1492
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds having the formula ##STR1## wherein X, R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6, and R.sup.7 are as defined herein as well as readily hydrolyzable esters thereof, pharmaceutically acceptable salts of said compounds and hydrates of the compounds of formula I and of their esters and salts.

These compounds have valuable pharmacological activity for the treatment and prophylaxis of infectious diseases, especially those caused by methicillin resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa.

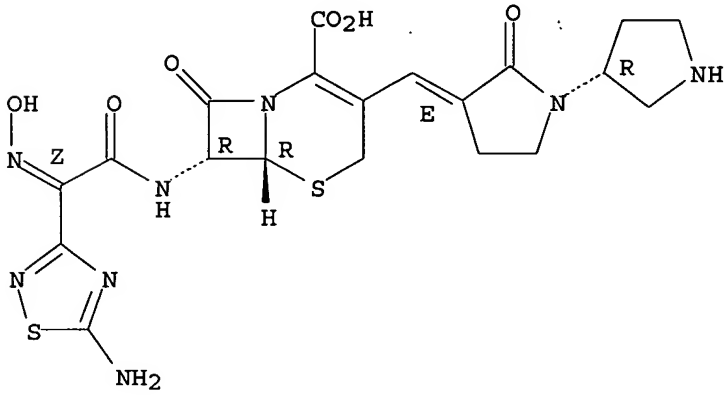
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **209467-52-7P**
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)

RN 209467-52-7 USPATFULL

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

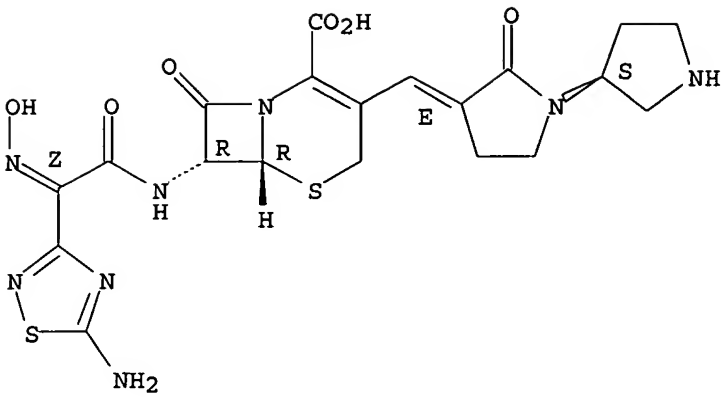


IT **209467-53-8P 209467-54-9P 209467-56-1P**
209467-60-7P 209467-61-8P 209467-62-9P
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)

RN 209467-53-8 USPATFULL

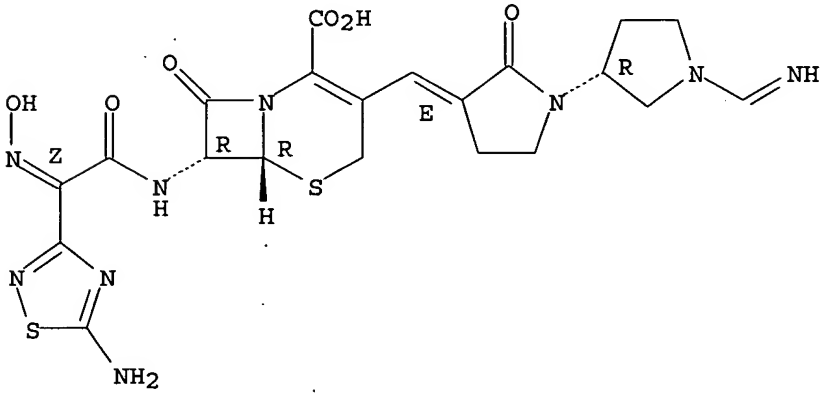
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'S)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



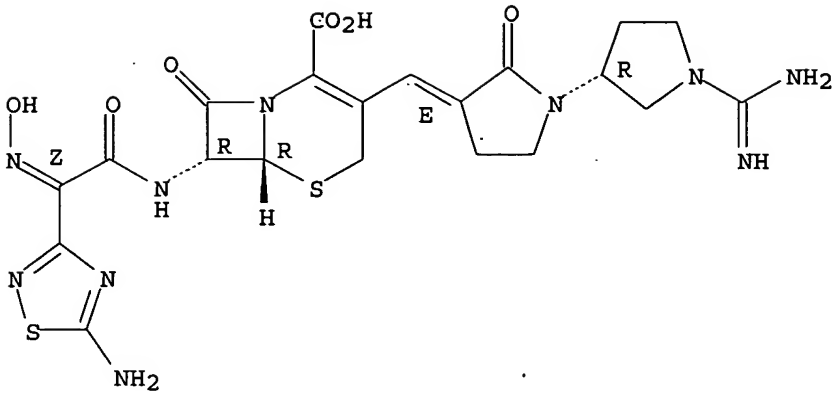
RN 209467-54-9 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-(iminomethyl)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



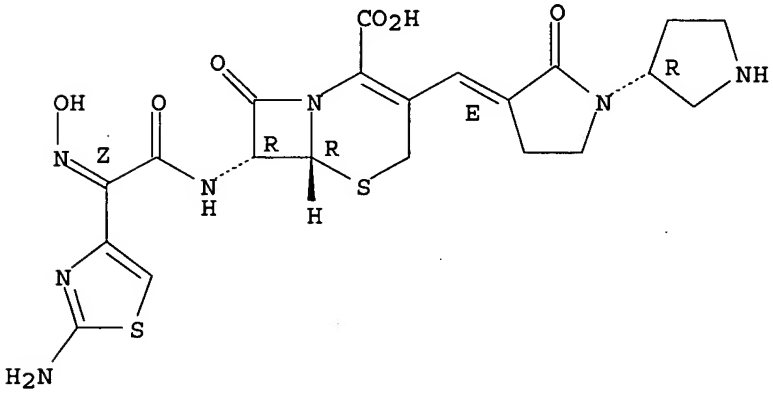
RN 209467-56-1 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(E)-[(3'R)-1'-(aminoiminomethyl)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



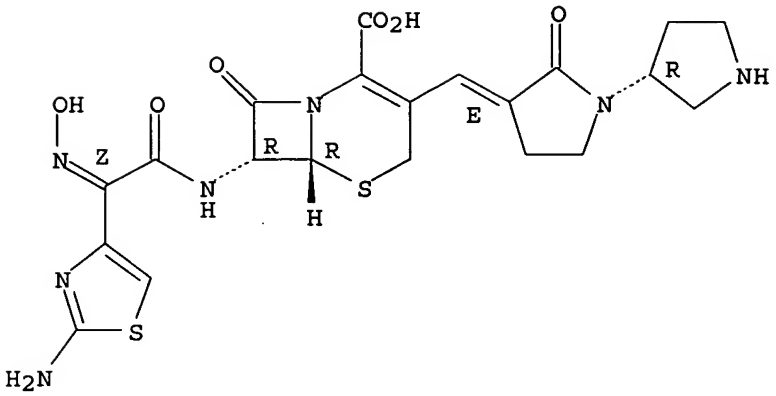
RN 209467-60-7 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209467-61-8 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, dihydrochloride, (6R,7R)- (9CI) (CA INDEX NAME)

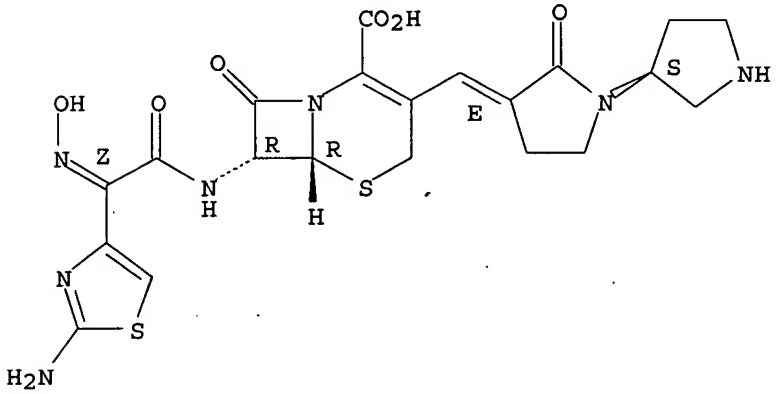
Absolute stereochemistry.
Double bond geometry as shown.



●2 HCl

RN 209467-62-9 USPATFULL
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'S)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, dihydrochloride, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



●2 HCl

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:52:48 ON 04 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 4 Aug 2005 VOL 143 ISS 6
FILE LAST UPDATED: 3 Aug 2005 (20050803/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l28

L28 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:817896 HCAPLUS
DN 141:337706
ED Entered STN: 07 Oct 2004
TI Cephalosporin in crystalline form
IN Berghausen, Joerg
PA **Basilea Pharmaceutica A.-G., Switz.**
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D501-56
ICS A61K031-545; A61K031-04
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 26, 75
FAN.CNT 1

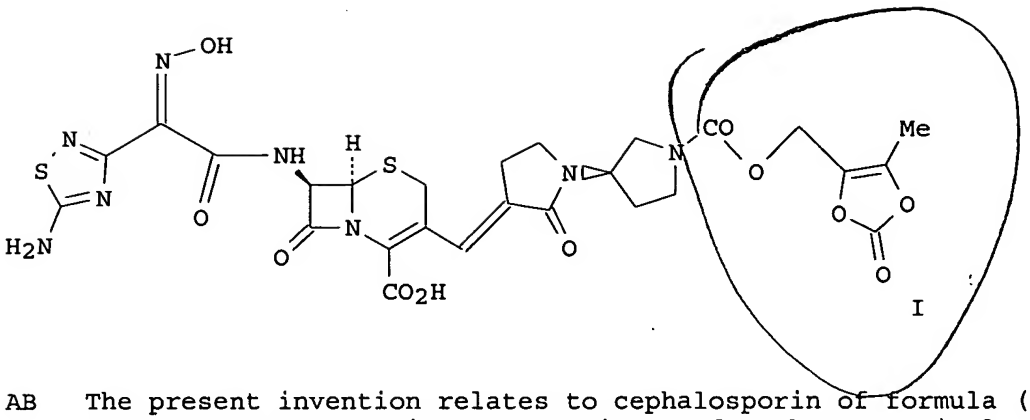
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004085444	A1	20041007	WO 2004-EP2667	20040315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-6815 A 20030327
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004085444	ICM	C07D501-56
	ICS	A61K031-545; A61K031-04
WO 2004085444	ECLA	C07D501/00

GI



AB The present invention relates to cephalosporin of formula (I) in crystalline form, a process for its preparation, and a pharmaceutical composition containing cephalosporin I in crystalline form. A process for the preparation of cephalosporin I crystalline form comprises (i) mixing an acid and an organic solvent, adding the solution to I-Na salt, and stirring the mixture, (ii) mixing an acid and an organic solvent, adding I-Na salt to the solution, and stirring the mixture., or (iii) suspending I-Na salt in water and an acid and stirring the mixture The compound of formula I in crystalline form is useful as antibiotics having potent and broad antibacterial activity, especially against methicillin-resistant Staphylococci (MRSA) and Pseudomonas aeruginosa.

ST cephalosporin cryst form prepn delivery system

IT Antibacterial agents
Antibiotics
Crystallization
Drug delivery systems
(preparation of cephalosporin in crystalline form for dosage forms)

IT **768386-94-3P**
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(amorphous and crystalline; preparation of cephalosporin in crystalline form for dosage forms)

IT **252188-71-9**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(amorphous; preparation of cephalosporin in crystalline form for dosage forms)

IT **376653-43-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous; preparation of cephalosporin in crystalline form for dosage forms)

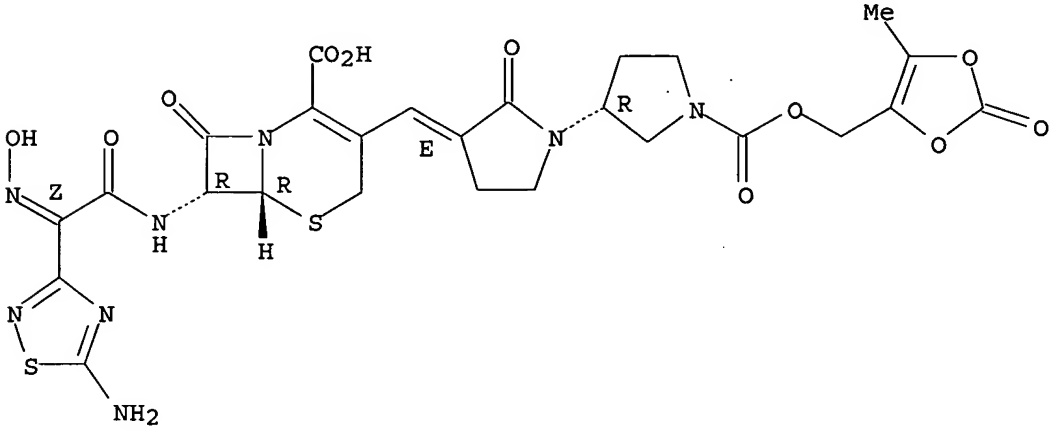
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Hebeisen, P; US 6232306 B1 2001 HCAPLUS
(2) Hoffmann La Roche; EP 1087980 A 2001 HCAPLUS

IT **768386-94-3P**
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(amorphous and crystalline; preparation of cephalosporin in crystalline form for

dosage forms)
RN 768386-94-3 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monohydrochloride, (6R,7R)- (9CI) (CA INDEX NAME)

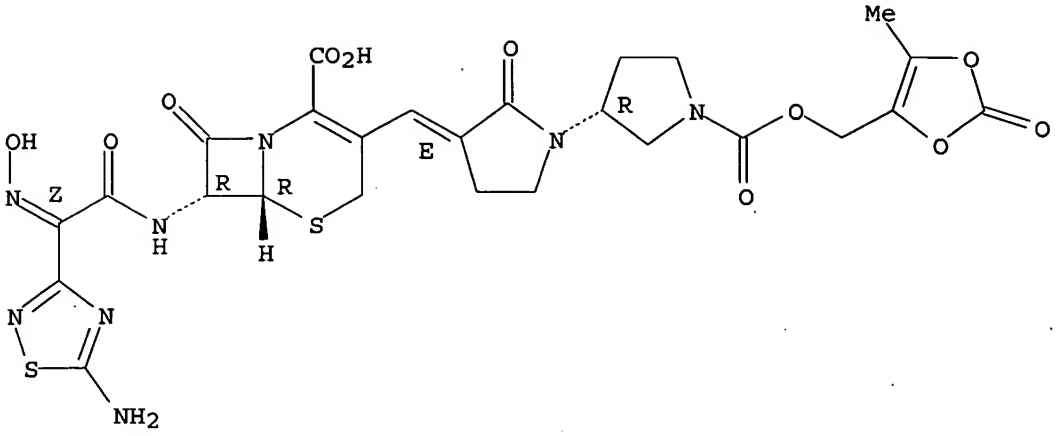
Absolute stereochemistry.
Double bond geometry as shown.



● HCl

IT **252188-71-9**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(amorphous; preparation of cephalosporin in crystalline form for dosage forms)
RN 252188-71-9 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

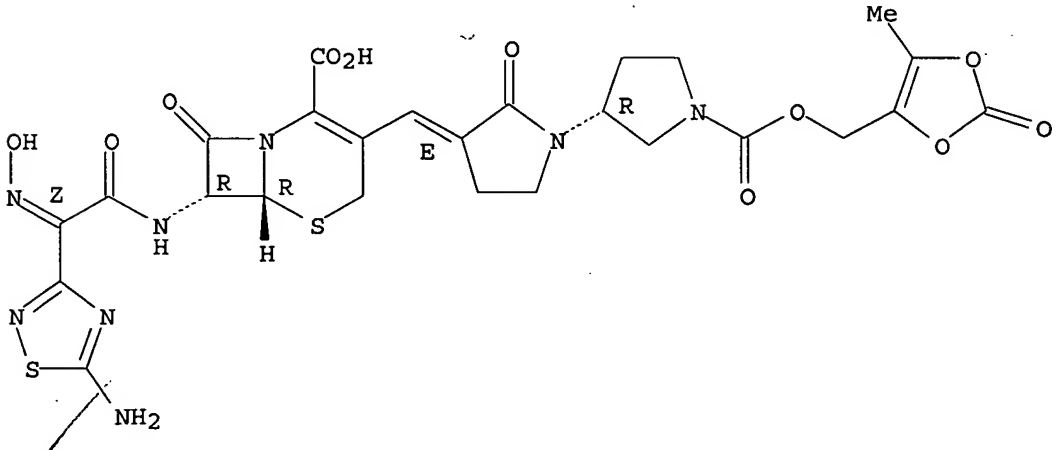
Absolute stereochemistry.
Double bond geometry as shown.



● Na

IT **376653-43-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous; preparation of cephalosporin in crystalline form for dosage forms)
RN 376653-43-9 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L28 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:551566 HCAPLUS
DN 141:199419
ED Entered STN: 09 Jul 2004
TI Multiple-dose pharmacokinetics and safety of a novel broad-spectrum cephalosporin (**BAL5788**) in healthy volunteers

AU Schmitt-Hoffmann, Anne; Nyman, Lars; Roos, Brigitte; Schleimer, Michael; Sauer, Jill; Nashed, Norman; Brown, Thomas; Man, Anthony; Weidekamm, Erhard

CS **Basilea Pharmaceuticals Ltd., Basel, 4002, Switz.**

SO Antimicrobial Agents and Chemotherapy (2004), 48(7), 2576-2580
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
CC 1-2 (Pharmacology)

AB **BAL5788** is the water-soluble prodrug of **BAL9141**, a novel broad-spectrum cephalosporin with potent bactericidal activity against methicillin-resistant Staphylococcus aureus (MRSA) and penicillin-resistant Streptococcus pneumoniae. Safety and pharmacokinetic data from a multiple-dose study with 16 healthy male volunteers are reported. Subjects were randomized to receive **BAL5788** at 500 or 750 mg (as **BAL9141** equiv; n = 6 subjects per dose) or placebo (n = 2 subjects per dose). The doses were given as 200-mL infusions over 30 min once daily on days 1 and 8 and twice daily on days 2 to 7. **BAL5788** was well tolerated, with no severe or serious adverse events (AEs) or dosing-related changes in laboratory parameters, electro-cardiog. findings, or vital signs. Drug accumulation in plasma was negligible during the dosing period. The results of pharmacokinetic analyses agreed well with data reported from a previous single-ascending-dose study. The elimination half-life of **BAL9141** was about 3 h. The volume of distribution at steady state was equal to the volume of the adult extracellular water compartment. **BAL9141** was predominantly eliminated in urine, and renal clearance of the free drug corresponded to the normal glomerular filtration rate in adults. After multiple infusions of 750 mg, the mean concns. of **BAL9141** in plasma exceeded the MIC at which 100% of MRSA isolates are inhibited (4 μg/mL) for approx. 7 to 9 h, corresponding to 58 to 75% of a 12-h dosing interval.

ST antibacterial **BAL5788** pharmacokinetics safety

IT Human
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

IT **252188-71-9**, BAL 5788
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

IT **209467-52-7**, **BAL9141**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Alexander, J; J Med Chem 1996, V39, P480 HCAPLUS
(2) Cars, O; Diagn Microbiol Infect Dis 1997, V27, P29 HCAPLUS
(3) Chew, T; J Clin Microbiol 1992, V30, P3028 MEDLINE
(4) Craig, W; Clin Infect Dis 2001, V33(Suppl 2), P233
(5) Entenza, J; Antimicob Agents Chemother 2002, V46, P171 HCAPLUS
(6) Fuchs, P; Antimicrob Agents Chemother 2000, V44, P2880 HCAPLUS
(7) Hebeisen, P; Antimicob Agents Chemother 2001, V45, P825 HCAPLUS
(8) Jones, R; J Antimicrob Ther 2002, V50, P915 HCAPLUS
(9) Klepser, M; Clin Pharmacokinet 1995, V28, P361 HCAPLUS
(10) Mouton, J; J Antimicrob Chemother 2001, V47, P500 HCAPLUS
(11) National Nosocomial Infections Surveillance System; Am J Infect Control 2001, V29, P404

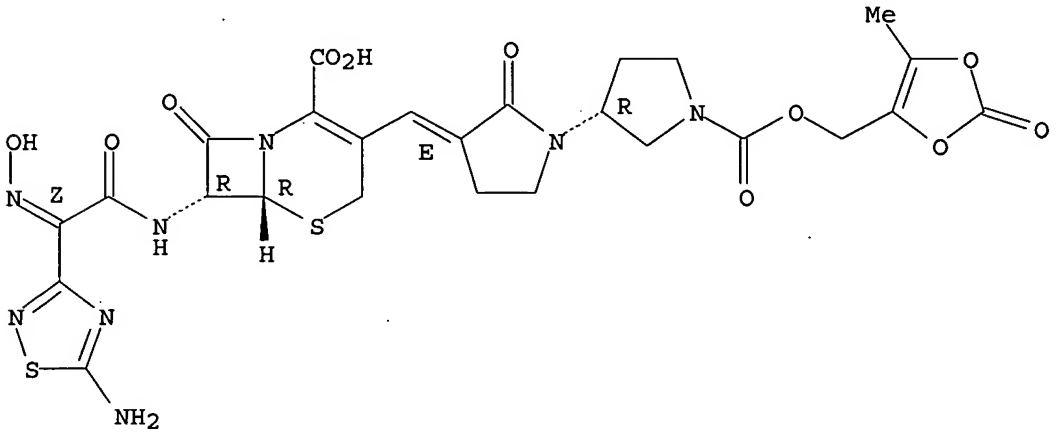
(12) Nix, D; Antimicrob Agents Chemother 1991, V35, P1947 HCAPLUS
(13) Rogerson, F; J Agric Food Chem 2001, V49, P263 HCAPLUS
(14) Schmitt-Hoffmann, A; Antimicob Agents Chemother 2004, V48, P2570 HCAPLUS
(15) Sievert, D; Morb Mortal Wkly Rep 2002, V51, P565
(16) Sorgel, F; J Antimicrob Chemother 1993, V31, P39
(17) Tsiodras, S; Lancet 2001, V358, P207 HCAPLUS

IT **252188-71-9**, BAL 5788
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

RN 252188-71-9 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

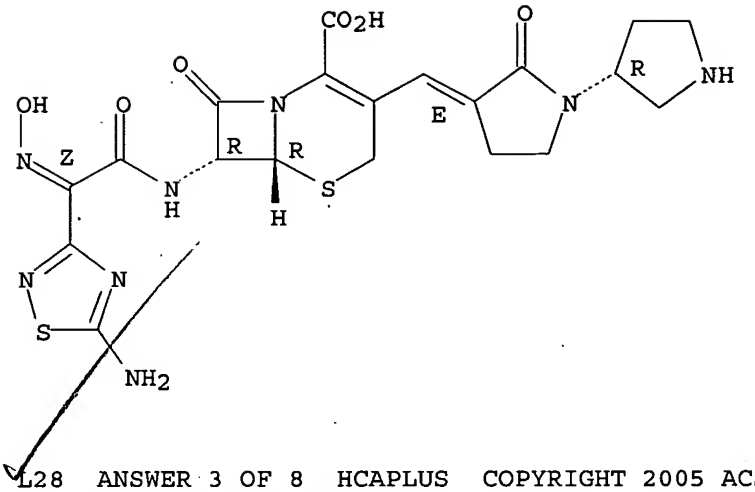


IT **209467-52-7**, **BAL9141**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

RN 209467-52-7 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L28 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:551565 HCAPLUS
DN 141:184564
ED Entered STN: 09 Jul 2004
TI Single-dose pharmacokinetics and safety of a novel broad-spectrum cephalosporin (**BAL5788**) in healthy volunteers
AU Schmitt-Hoffmann, Anne; Roos, Brigitte; Schleimer, Michael; Sauer, Jill; Man, Anthony; Nashed, Norman; Brown, Thomas; Perez, Antonio; Weidekamm, Erhard; Kovacs, Peter
CS **Basilea Pharmaceutica Ltd., Basel, Switz.**
SO Antimicrobial Agents and Chemotherapy (2004), 48(7), 2570-2575
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
CC 1-2 (Pharmacology)
AB **BAL5788** is the water-soluble prodrug of **BAL9141**, a novel broad-spectrum cephalosporin with potent bactericidal activities against methicillin-resistant Staphylococcus aureus (MRSA) and penicillin-resistant Streptococcus pneumoniae. We investigated the safety and pharmacokinetics of **BAL5788** in a double-blind, single-ascending-dose study with 40 healthy male subjects. The subjects were randomized to receive placebo (n = 2 subjects per dose) or **BAL5788** (n = 6 subjects per dose) as a 200-mL i.v. infusion over 30 min. The **BAL5788** doses used were 125, 250, 500, 750, and 1,000 mg (**BAL9141** equiv). All doses were well tolerated, with no severe or serious adverse events (AEs). The most frequent AE was taste disturbance. No electrocardiog. abnormalities and no trends or clin. significant changes in laboratory parameters or vital signs were observed The maximum concentration of drug in serum and the area under the concentration-time curve for **BAL9141** were dose proportional over the dosing range. The elimination half-life of **BAL9141** was about 3 h. The volume of distribution at steady state was equal to the volume of the adult extracellular water compartment, and the rate of renal clearance of free drug corresponded to the normal glomerular filtration rate for adults. More than 70% of the administered dose was excreted as **BAL9141** in the urine, and almost no prodrug was detected. After the infusion of 750 mg, the mean plasma **BAL9141** concns. exceeded the MIC at which 100% of MRSA isolates are inhibited (4 μg/mL) for approx. 7 h, or 58% of a 12-h dosing interval. These results indicate that infusions of

750 mg twice a day should be adequate for the treatment of infections caused by MRSA.

ST antibacterial cephalosporin **BAL5788** pharmacokinetics metab safety

IT Human
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

IT **252188-71-9**
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

IT **209467-52-7, BAL9141**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

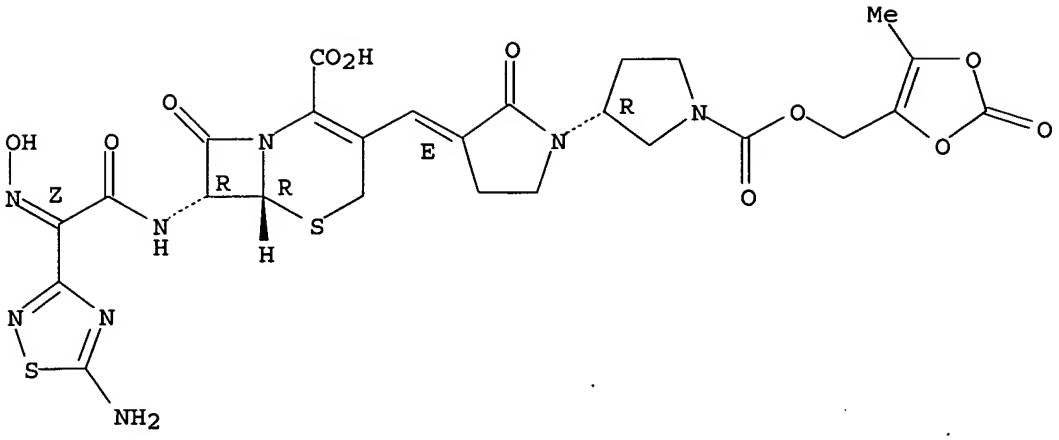
(1) Alexander, J; J Med Chem 1996, V39, P480 HCAPLUS
(2) Cars, O; Diagn Microbiol Infect Dis 1997, V27, P29 HCAPLUS
(3) Chew, T; J Clin Microbiol 1992, V30, P3028 MEDLINE
(4) Craig, W; Clin Infect Dis 2001, V33(Suppl 2), P233
(5) Dancer, S; J Antimicrob Chemother 2001, V48, P463 HCAPLUS
(6) Daum, S; Crit Care Med 2001, V29(4 Suppl), PN92
(7) Diekema, D; Clin Infect Dis 2001, V32(Suppl 2), PS114
(8) Entenza, J; Antimicob Agents Chemother 2002, V46, P171 HCAPLUS
(9) Fuchs, P; Antimicrob Agents Chemother 2000, V44, P2880 HCAPLUS
(10) Glinka, T; Curr Opin Investig Drugs 2002, V3, P206 HCAPLUS
(11) Haley, R; Ann Intern Med 1982, V97, P297 MEDLINE
(12) Hebeisen, P; Antimicrob Agents Chemother 2001, V45, P825 HCAPLUS
(13) Jones, R; J Antimicrob Ther 2002, V50, P915 HCAPLUS
(14) Klepser, M; Clin Pharmacokinet 1995, V28, P361 HCAPLUS
(15) Mouton, J; J Antimicrob Chemother 2001, V47, P500 HCAPLUS
(16) National Nosocomial Infections Surveillance System; Am J Infect Control 2001, V29, P404
(17) Nix, D; Antimicrob Agents Chemother 1991, V35, P1947 HCAPLUS
(18) Panlilio, A; Infect Control Hosp Epidemiol 1992, V13, P582 MEDLINE
(19) Rogerson, F; J Agric Food Chem 2001, V49, P263 HCAPLUS
(20) Rybak, M; Drugs 2001, V61, P1 HCAPLUS
(21) Sievert, D; Morb Mortal Wkly Rep 2002, V51, P565
(22) Sorgel, F; J Antimicrob Chemother 1993, V31, P39
(23) Tsiodras, S; Lancet 2001, V358, P207 HCAPLUS

IT **252188-71-9**
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)

RN 252188-71-9 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

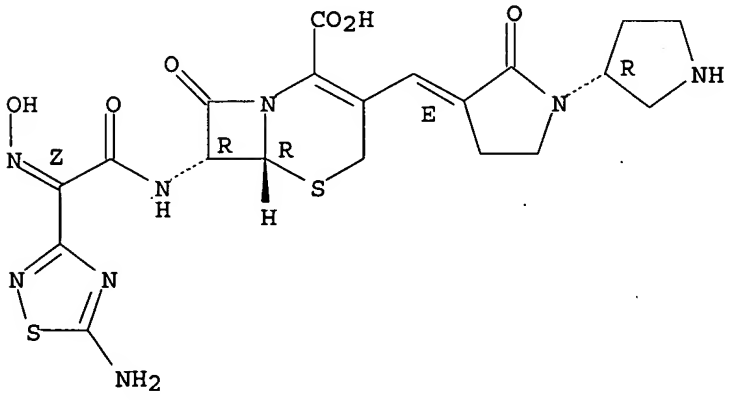
Absolute stereochemistry.
Double bond geometry as shown.



● Na

IT **209467-52-7, BAL9141**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetics and safety of **BAL5788** in healthy volunteers)
RN 209467-52-7 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L28 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:120824 HCAPLUS
DN 140:163625
ED Entered STN: 13 Feb 2004
TI Process for the preparation of amino-pyrrolidine derivatives for use as intermediates in cephalosporin synthesis
IN **Muller, Marc; Soukup, Milan**

PA **Basilea Pharmaceutica AG, Switz.**
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D207-14
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 27

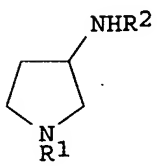
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2004013097	A1	20040212	WO 2003-EP8132	20030724	<--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
	CA 2491133	AA	20040212	CA 2003-2491133	20030724	<--
	EP 1546096	A1	20050629	EP 2003-766281	20030724	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
	BR 2003013355	A	20050712	BR 2003-13355	20030724	<--
	US 2004034236	A1	20040219	US 2003-629483	20030729	<--
	US 6872836	B2	20050329			
	US ~~2004127703~~	A1	20040701	US 2003-743365	20031222	<--
PRAI	EP 2002-16944	A	20020801	<--		
	WO 2003-EP8132	W	20030724			
	US 2003-629483	A3	20030729	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 2004013097	ICM	C07D207-14	
WO 2004013097	ECLA	C07D207/14	<--
BR 2003013355	ECLA	C07D207/14	<--
US 2004034236	NCL	548/531.000; 548/557.000	
	ECLA	C07D207/14	<--
US 2004127703	NCL	540/222.000	
	ECLA	C07D207/14	<--

OS CASREACT 140:163625; MARPAT 140:163625
GI



AB This invention is concerned with a process for the manufacture of optically active 3-amino-pyrrolidines, such as I [R1, R2 = H, amino protecting group], for use as intermediates for the production of agrochems. and of pharmaceutically active substances such as, vinylpyrrolidinone-

cephalosporin derivs. Thus, (R)-3-amino-N-(tert-butoxycarbonyl)pyrrolidine (II) was prepared via cyclocondensation of (R)-2-(benzyloxycarbonylamino)-1,4-dimethanesulfonyloxybutane with hydroxylamine hydrochloride by heating at 60° overnight in a 1:1 mixture of Et3N and DMSO to give (R)-3-(benzyloxycarbonylamino)-N-hydroxypyrrolidine (III) in 85% yield. III was hydrogenated using Raney Ni in EtOH and the in situ formed partially deprotected pyrrole was treated with di-tert-butyldicarbonate to give (R)-3-(benzyloxycarbonylamino)-N-(tert-butoxycarbonyl)pyrrolidine(IV) in 81% yield. IV was then hydrogenated using Pd/C in EtOH to give the desired partially deprotected II. II has been shown to be a useful intermediate for the preparation of **Ro 63-9141**, a cephalosporin antibiotic.

ST beta lactam antibiotic cephalosporin amino pyrrolidine deriv prepn; asym synthesis cephalosporin amino pyrrolidine deriv

IT Asymmetric synthesis and induction
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT Lactams
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(β-, antibiotics; process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT Antibiotics
(β-lactam; process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT 7440-02-0, Raney nickel, uses
RL: CAT (Catalyst use); USES (Uses)
(catalysts; process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT 7440-05-3, Palladium, uses
RL: CAT (Catalyst use); USES (Uses)
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT 11111-12-9DP, Cephalosporin, amino-pyrrolidine derivs.
209467-52-7P
RL: **IMF (Industrial manufacture); PNU (Preparation, unclassified); PREP (Preparation)**
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT 147081-49-0P, (R)-3-Amino-N-(tert-butoxycarbonyl)pyrrolidine
655785-23-2P, (R)-3-(Benzyloxycarbonylamino)-N-hydroxypyrrolidine
655785-25-4P, (R)-3-(Benzyloxycarbonylamino)-N-(tert-butoxycarbonyl)pyrrolidine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

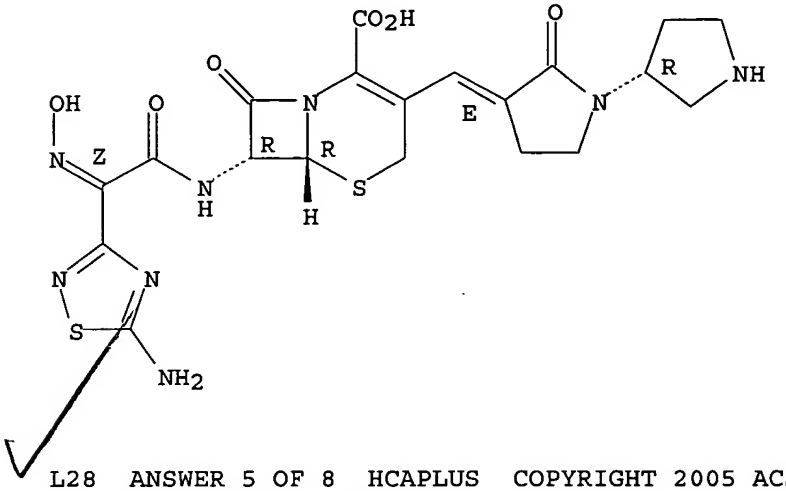
IT 5470-11-1, Hydroxylamine hydrochloride 24424-99-5, Di-tert-butyldicarbonate 655785-24-3, (R)-2-(Benzyloxycarbonylamino)-1,4-dimethanesulfonyloxybutane
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

IT **209467-52-7P**
RL: **IMF (Industrial manufacture); PNU (Preparation, unclassified); PREP (Preparation)**
(process for asym. synthesis of cephalosporin amino-pyrrolidine derivs.)

RN 209467-52-7 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L28 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:868457 HCAPLUS
DN 136:5852
ED Entered STN: 30 Nov 2001
TI New process for the preparation of vinyl-pyrrolidinone cephalosporin derivatives
IN Hebeisen, Paul; Hilpert, Hans; Humm, Roland
PA **Basilea Pharmaceutica A.-G., Switz.**
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D501-00
ICS C07F009-572
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 10
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090111	A1	20011129	WO 2001-EP5721	20010518 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002019381	A1	20020214	US 2001-860157	20010517 <--
	US 6504025	B2	20030107		
	CA 2408941	AA	20011129	CA 2001-2408941	20010518 <--
	EP 1289998	A1	20030312	EP 2001-936374	20010518 <--
	EP 1289998	B1	20050330		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

```
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2003535059          T2     20031125    JP 2001-586298          20010518 <--
     EP 1435357             A2     20040707    EP 2004-2120            20010518 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI, CY, TR
     AT 292135              E      20050415    AT 2001-936374          20010518 <--
PRAI EP 2000-111164         A      20000524  <--
     EP 2001-936374         A3     20010518  <--
     WO 2001-EP5721         W      20010518  <--
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------   -----  ----------------------------------------------
 WO 2001090111    ICM    C07D501-00
                  ICS    C07F009-572
 WO 2001090111    ECLA   C07D501/00; C07F009/572K4; C07F009/6558B;
                         C07F009/6558C; C07F009/6561B                    <--
 US 2002019381    NCL    540/222.000; 540/228.000
                  ECLA   C07D501/00; C07F009/572K4; C07F009/6558B;
                         C07F009/6558C; C07F009/6561B                    <--
 EP 1435357       ECLA   C07D501/00; C07F009/572K4; C07F009/6558B; C07F009/6558C
                                                                         <--
OS   CASREACT 136:5852; MARPAT 136:5852
GI
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing pharmaceutic compns., a vinyl-pyrrolidinone cephalosporin derivative of I via the acylation of deacetyl-7-aminocephalosporanic acid with II (R1 = a hydroxy protecting group; Y1-Y3 = an activating group) in base followed by the protection of the carboxylic acid group, formation of an aldehyde at C3 using an inorg. hypohalite in TEMPO or with MnO2, and reacting the aldehyde with III (R = an amino protecting group or group A), was accomplished. I can be used for the treatment and prophylaxis of infectious diseases, especially infectious diseases caused by bacterial pathogens in particular methicillin resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa (no data).

ST cephalosporin vinyl pyrrolidinone deriv prepn; beta lactam vinyl pyrrolidinone deriv prepn

IT Infection
(bacterial; process for preparing pyrrolidinone cephalosporin derivs.)

IT Pathogen
(process for preparing pyrrolidinone cephalosporin derivs.)

IT Lactams
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(β-; process for preparing pyrrolidinone cephalosporin derivs.)

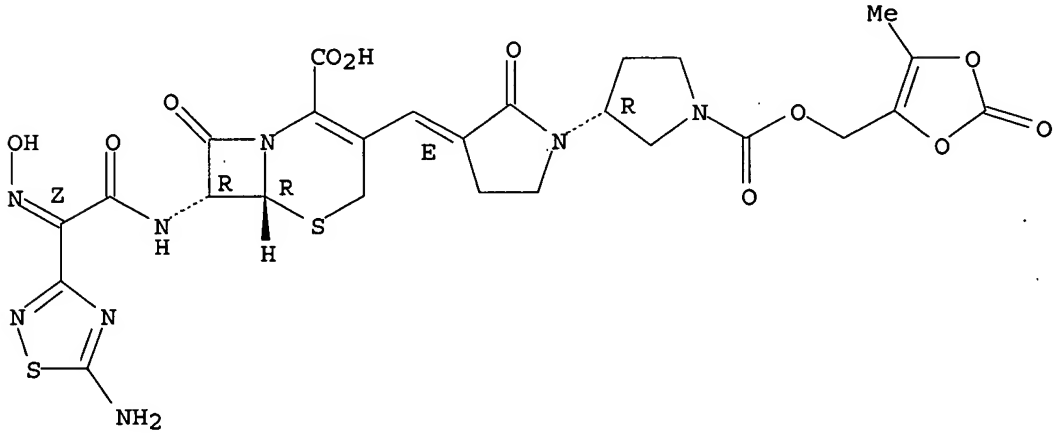
IT 376653-40-6P 376653-41-7P **376653-43-9P**
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(process for preparing pyrrolidinone cephalosporin derivs.)

IT 80-70-6, 1,1,3,3-Tetramethylguanidine 15690-38-7 173604-87-0 209467-59-4 209468-02-0 252188-82-2 376653-42-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing pyrrolidinone cephalosporin derivs.)

IT **209467-52-7P** 376653-36-0P 376653-37-1P 376653-38-2P 376653-39-3P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP**

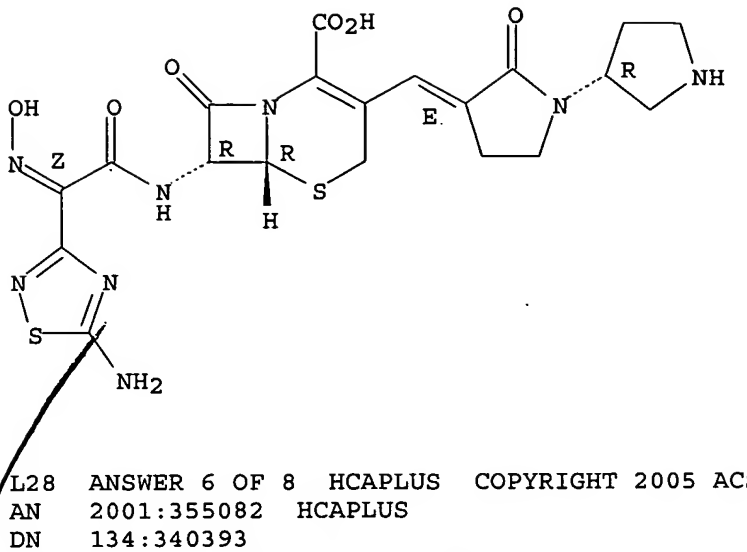
(Preparation); RACT (Reactant or reagent)
(process for preparing pyrrolidinone cephalosporin derivs.)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hoffmann-La Roche; EP 0812846 A 1997 HCAPLUS
(2) Hoffmann-La Roche; EP 0849269 A 1998 HCAPLUS
(3) Hoffmann-La Roche; WO 9965920 A 1999 HCAPLUS
IT **376653-43-9P**
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(process for preparing pyrrolidinone cephalosporin derivs.)
RN 376653-43-9 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **209467-52-7P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(process for preparing pyrrolidinone cephalosporin derivs.)
RN 209467-52-7 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



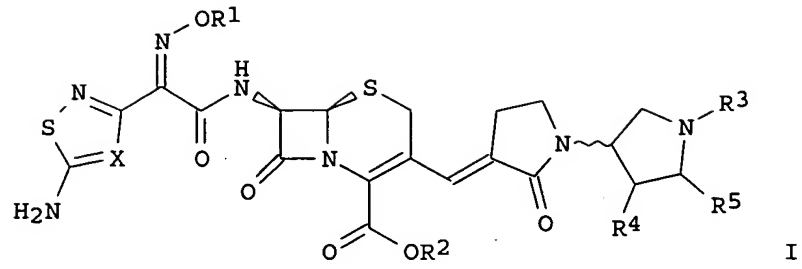
L28 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:355082 HCAPLUS
DN 134:340393
ED Entered STN: 17 May 2001
TI Preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cepham derivatives for the treatment of bacterial infections
IN Hebeisen, Paul; Hubschwerlen, Christian; Specklin, Jean-luc
PA Hoffmann-La Roche Inc., USA
SO U.S., 9 pp., Cont.-in-part of U.S. Ser. No. 315,715.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D501-24
ICS A61K031-546; A61P031-04
INCL 514202000
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 10
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 6232306	B1	20010515	US 1999-332811	19990614	<--
	TR 200003654	T2	20010321	TR 2000-200003654	19990607	<--
	ZA 2000006960	A	20020227	ZA 2000-6960	20001127	<--
PRAI	EP 1998-110888	A	19980615	<--		
	EP 1998-117099	A	19980910	<--		
	US 1999-315715	A2	19990520	<--		

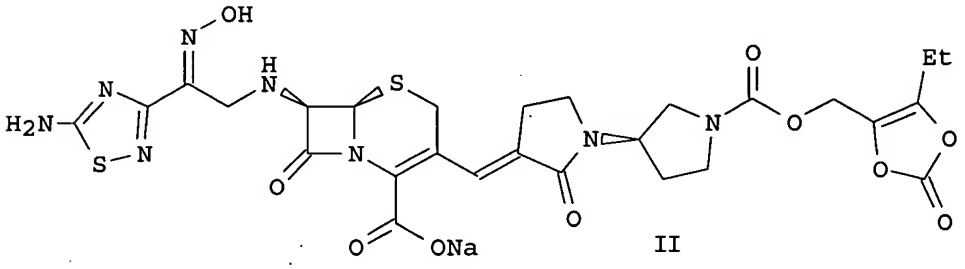
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
US 6232306	ICM	C07D501-24	
	ICS	A61K031-546; A61P031-04	
	INCL	514202000	
US 6232306	NCL	514/202.000; 540/222.000	
	ECLA	C07D501/00	<--

OS MARPAT 134:340393
GI



I



II

AB 3-(2-Oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams [I; R1 = H, alkyl, cycloalkyl; R2 = H, -CH2C(=CHR)-CO2R, -CH2OCOR, -CH(R)OCOR, -CH(R)OCO2R, -CH(OCOR)OCOR, -CH2COCH2OCOR and 2-oxo-1,3-dioxol-4-ylmethyl; R3 = H, -CH2C(=CH2)-CO2R, -CO2CH2C(=CHR)-CO2R, -CO2CH2OCOR, -CO2CH(R)OCOR, -COCH(R)OCO2R, -CO2CH(OCOR)OCOR, -CO2CH2COCH2OCOR, 2-oxo-1,3-dioxol-4-ylmethyloxycarbonyl; R = H, alkyl; R4 = H, OH; R5 = H, hydroxyalkyl; X = CH, N] and their pharmaceutically acceptable salts and hydrates were prepared for their use in the treatment and prophylaxis of infectious diseases (no data). Thus, cephem II was prepared via N-acylation of (6R,7R)-7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid with carbonic acid (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-nitrophenyl ester.

ST cephem prepn antibacterial

IT Antibacterial agents
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)

IT Lactams
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β-; preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)

IT **252188-71-9P 252188-72-0P 252188-73-1P**
252188-74-2P 252188-75-3P 252188-78-6P
252188-80-0P 252188-84-4P **338392-90-8P** 338392-98-6P
338393-01-4P 338393-03-6P 338393-04-7P 338393-06-9P 338393-08-1P
338393-24-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)

IT 7693-46-1 10029-04-6 24424-99-5, Di-tert-butyldicarbonate
124084-55-5 173604-87-0 **209467-52-7** 338393-16-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)

IT 252188-82-2P 252188-93-5P 338393-20-7P 338393-26-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

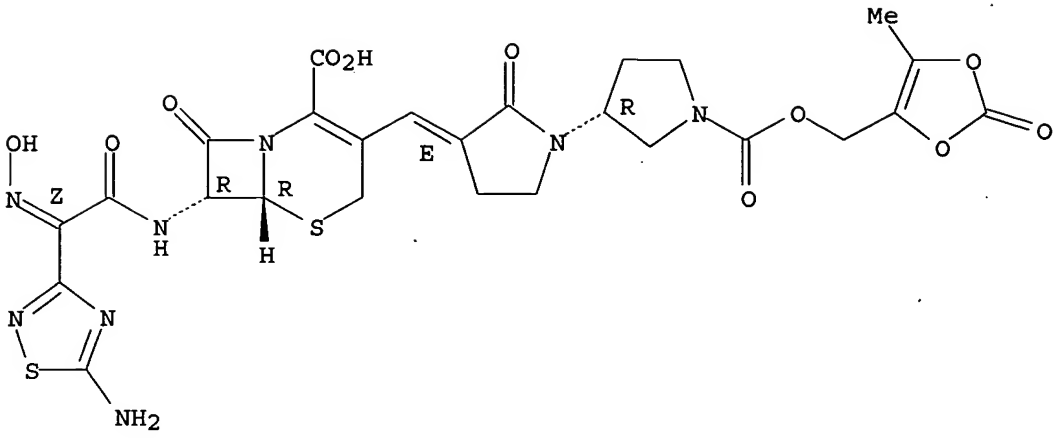
(1) Alexander; US 5466811 1995 HCAPLUS
(2) Angehrn; US 5981519 1999 HCAPLUS
(3) Anon; EP 0841339 1998 HCAPLUS
(4) Anon; EP 0849269 1998 HCAPLUS
(5) Cheng; US 5610314 1997 HCAPLUS
(6) Christian, H; The Journal of Antibiotics 1992, V45(8), P1358
(7) Jose, A; Journal of Medicinal Chemistry 1996, V39(2), P480
(8) Li, Z; Bioorganic and Medicinal Chemistry Letters 1997, V7(22), P2909 HCAPLUS

IT **252188-71-9P 252188-72-0P 252188-73-1P**
252188-74-2P 252188-75-3P 252188-78-6P
338392-90-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)

RN 252188-71-9 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

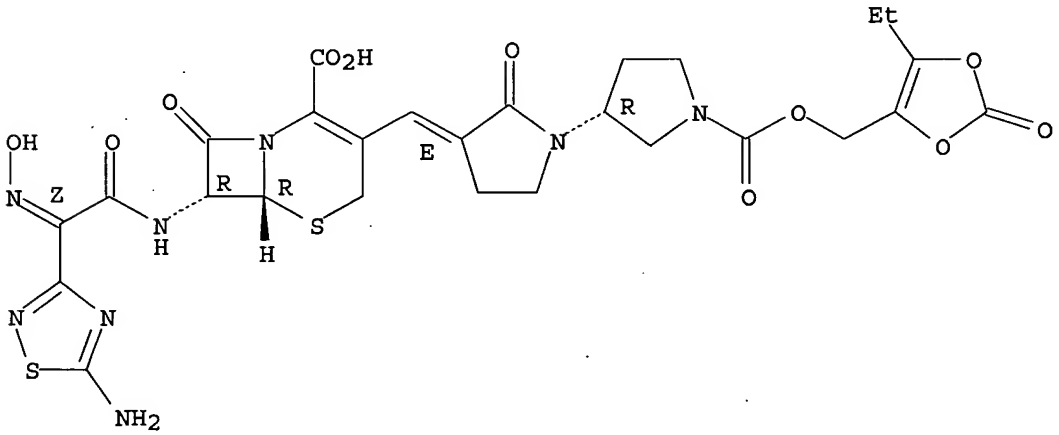
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-72-0 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-ethyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

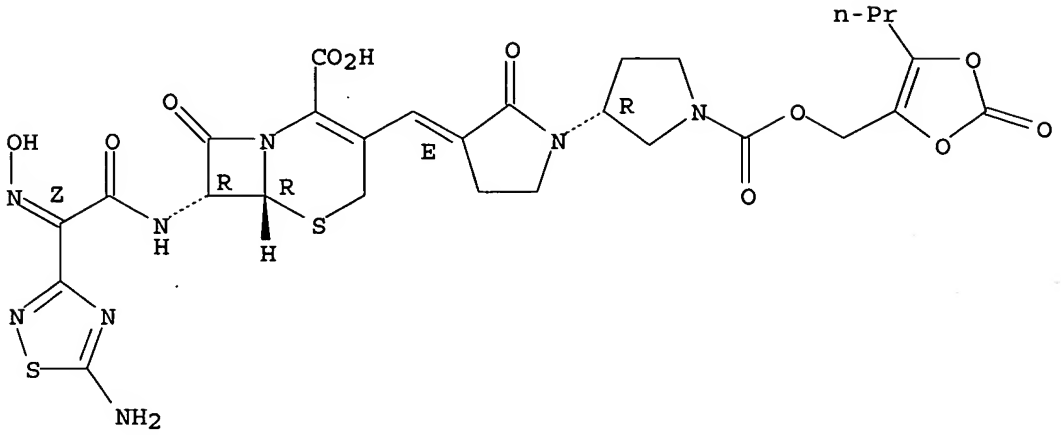


● Na

RN 252188-73-1 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo-1'-[[(2-oxo-5-propyl-1,3-dioxol-4-yl)methoxy]carbonyl][1,3'-bipyrrolidin]-3-ylidene]methyl]-, monosodium

salt, (6R,7R)- (9CI) (CA INDEX NAME)

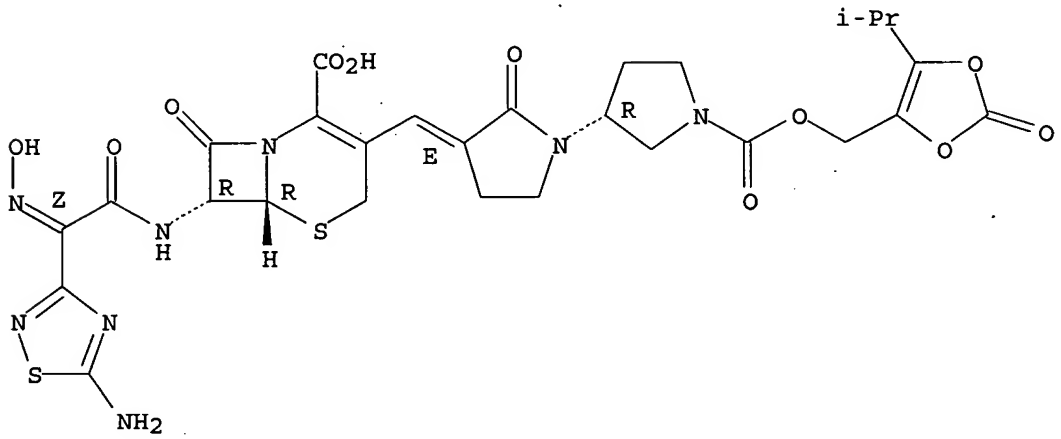
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-74-2 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[5-(1-methylethyl)-2-oxo-1,3-dioxol-4-yl]methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

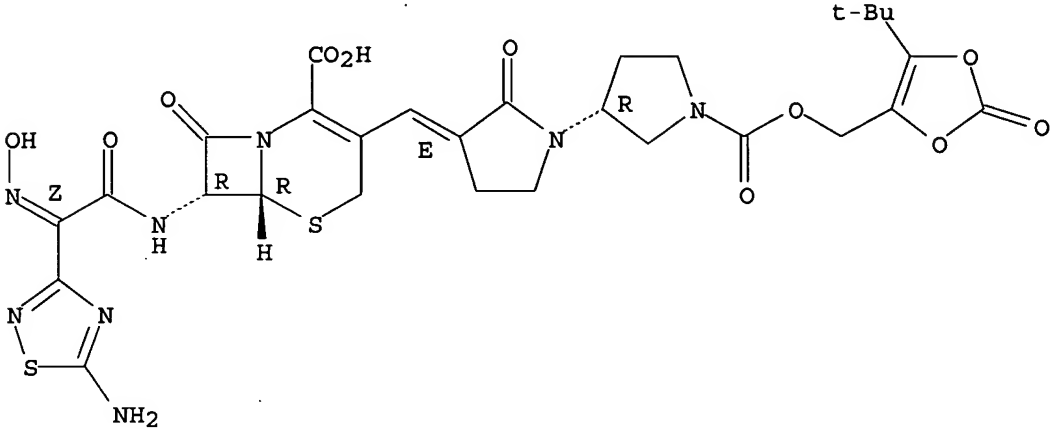


● Na

RN 252188-75-3 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[5-(1,1-dimethylethyl)-2-oxo-1,3-dioxol-4-yl]methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

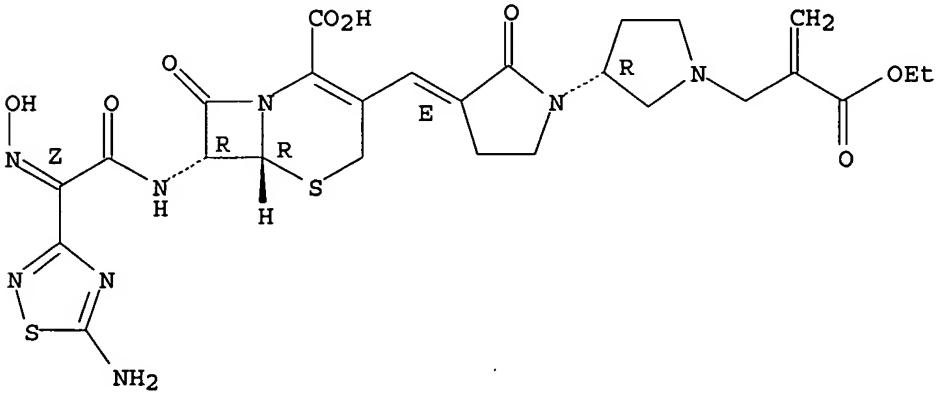
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-78-6 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[2-(ethoxycarbonyl)-2-propenyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

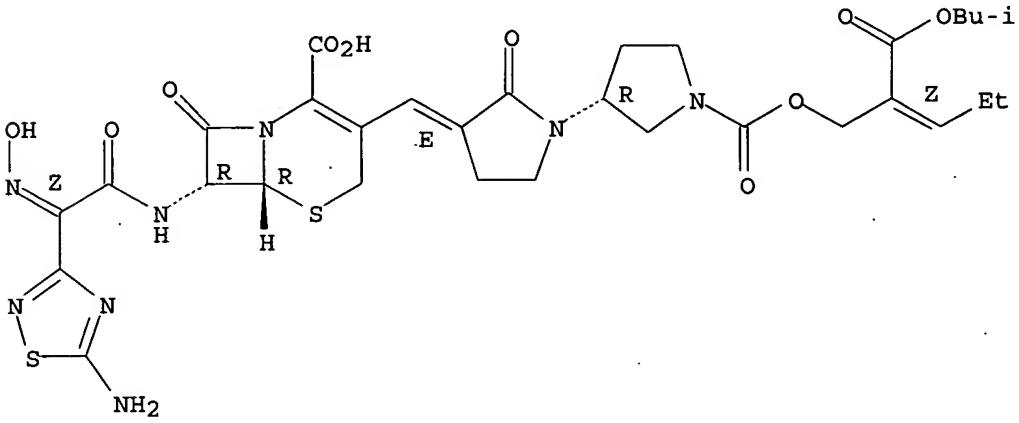
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 338392-90-8 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[(2Z)-2-[(2-methylpropoxy)carbonyl]-2-pentenyl]oxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)-(9CI) (CA INDEX NAME)

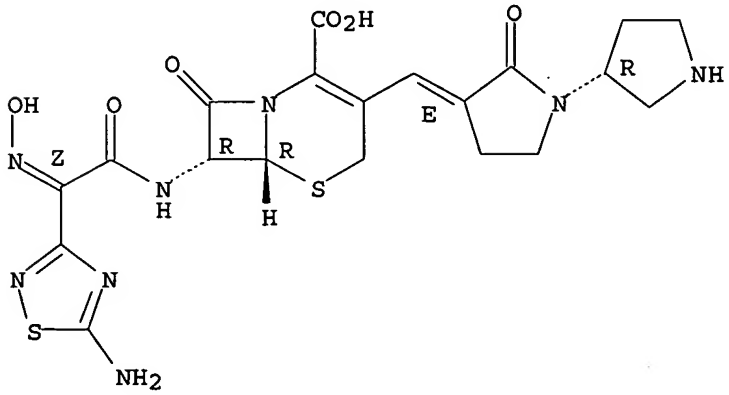
Absolute stereochemistry.
Double bond geometry as shown.



● Na

IT **209467-52-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephams for use as antibacterial agents)
RN 209467-52-7 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



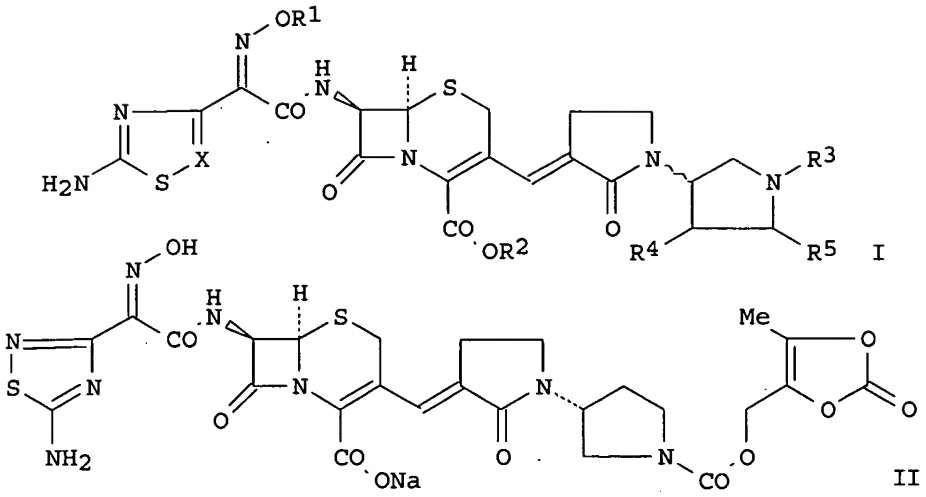
L28 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:811256 HCAPLUS
DN 132:22827
ED Entered STN: 24 Dec 1999
TI Preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics
IN Hebeisen, Paul; Hubschwerlen, Christian; Specklin, Jean-Luc
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D501-56
ICS A61K031-545
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 10, 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9965920	A1	19991223	WO 1999-EP3907	19990607 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2334568	AA	19991223	CA 1999-2334568	19990607 <--
AU 9945081	A1	20000105	AU 1999-45081	19990607 <--
AU 754732	B2	20021121		
BR 9911178	A	20010313	BR 1999-11178	19990607 <--
TR 200003654	T2	20010321	TR 2000-200003654	19990607 <--
EP 1087980	A1	20010404	EP 1999-927894	19990607 <--
EP 1087980	B1	20030129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002518401	T2	20020625	JP 2000-554745	19990607 <--
AT 231871	E	20030215	AT 1999-927894	19990607 <--
ES 2190222	T3	20030716	ES 1999-927894	19990607 <--
CN 1136221	B	20040128	CN 1999-807347	19990607 <--
ZA 2000006960	A	20020227	ZA 2000-6960	20001127 <--
NO 2000006350	A	20001213	NO 2000-6350	20001213 <--
PRAI EP 1998-110888	A	19980615	<--	
EP 1998-117099	A	19980910	<--	
WO 1999-EP3907	W	19990607	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9965920	ICM	C07D501-56
	ICS	A61K031-545
WO 9965920	ECLA	C07D501/00 <--
CN 1136221	ECLA	C07D501/00 <--

OS MARPAT 132:22827
GI



I

II

AB 3-(2-Oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems I [R1 = H, alkyl, cycloalkyl; R2 = H, Na, -CH2C(=CHR)-COOR, -CH2OCOR, -CH(R)OCOR, -CH(R)OCOOR, -CH(OCOR)OCOR, -CH2COCH2OCOR and 2-oxo-1,3-dioxol-4-ylmethyl; R3 =H, -CH2C(=CH2)-COOR, -COOCH2C(=CHR)-COOR, -COOCH2OCOR, -COOCH(R)OCOR, -CO CH(R)OCOOR, -COOCH(OCOR)OCOR, -COOCH2COCH2OCOR, 2-oxo-1,3-dioxol-4-ylmethyloxycarbonyl; R = H, alkyl; R4 = H, OH; R5 = H, hydroxyalkyl; X = CH, N] were prepared and formulated for use in the treatment and prophylaxis of infectious diseases (no data). Thus, cephem II was prepared via N-acylation of (6R,7R)-7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid with carbonic acid (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-nitrophenyl ester.

ST cephem prepn antibiotic

IT Antibiotics
(β-lactam; preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)

IT 252188-82-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)

IT **252188-71-9P 252188-72-0P 252188-73-1P**
252188-74-2P 252188-75-3P 252188-76-4P
252188-78-6P 252188-80-0P 252188-81-1P 252188-83-3P
252188-84-4P 252188-85-5P 252188-86-6P 252188-87-7P 252188-88-8P
252188-89-9P 252188-90-2P 252188-91-3P 252188-92-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)

IT 7693-46-1, 4-Nitrophenyl chloroformate 10029-04-6 124084-55-5
173604-87-0 **209467-52-7** 209468-80-4
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)

IT 252188-93-5P 252188-94-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Hoffmann La Roche; EP 0841339 A 1998 HCAPLUS

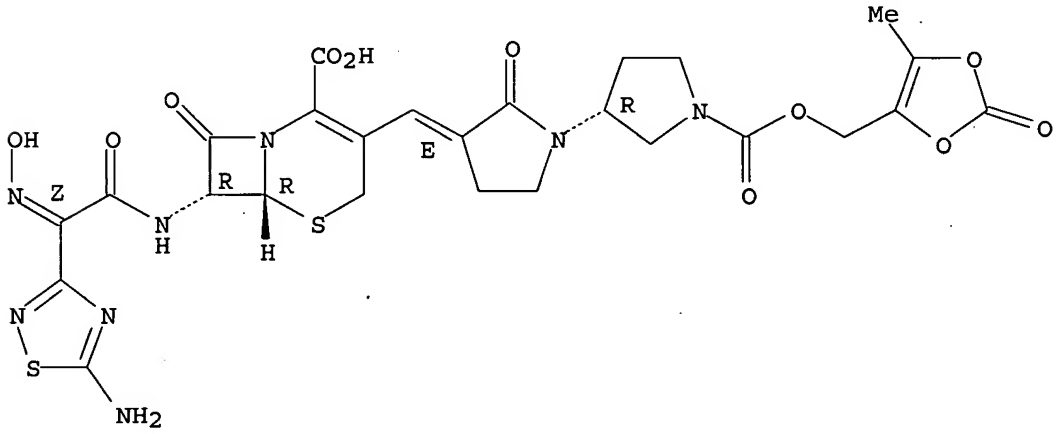
(2) Hoffmann La Roche; EP 0849269 A 1998 HCAPLUS

IT **252188-71-9P 252188-72-0P 252188-73-1P**
252188-74-2P 252188-75-3P 252188-76-4P
252188-78-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)

RN 252188-71-9 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



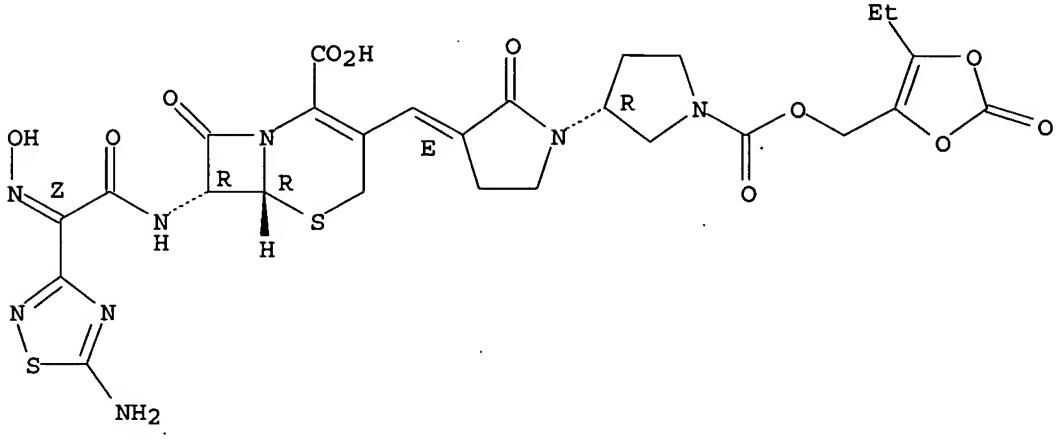
● Na

RN 252188-72-0 HCAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[(5-ethyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

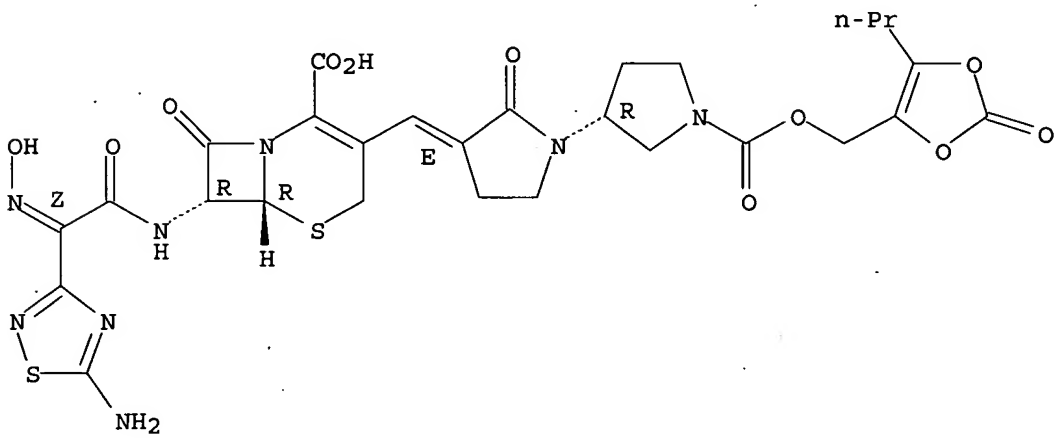
Double bond geometry as shown.



● Na

RN 252188-73-1 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo-1'-[[(2-oxo-5-propyl-1,3-dioxol-4-yl)methoxy]carbonyl][1,3'-bipyrrolidin]-3-ylidene]methyl]-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

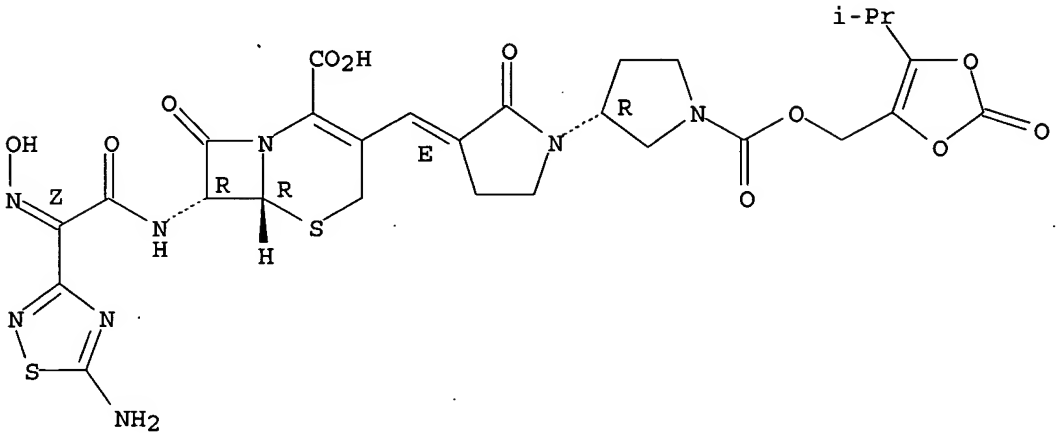


● Na

RN 252188-74-2 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[5-(1-methylethyl)-2-oxo-1,3-dioxol-4-yl]methoxy]carbonyl]-2-

oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)-
(9CI) (CA INDEX NAME)

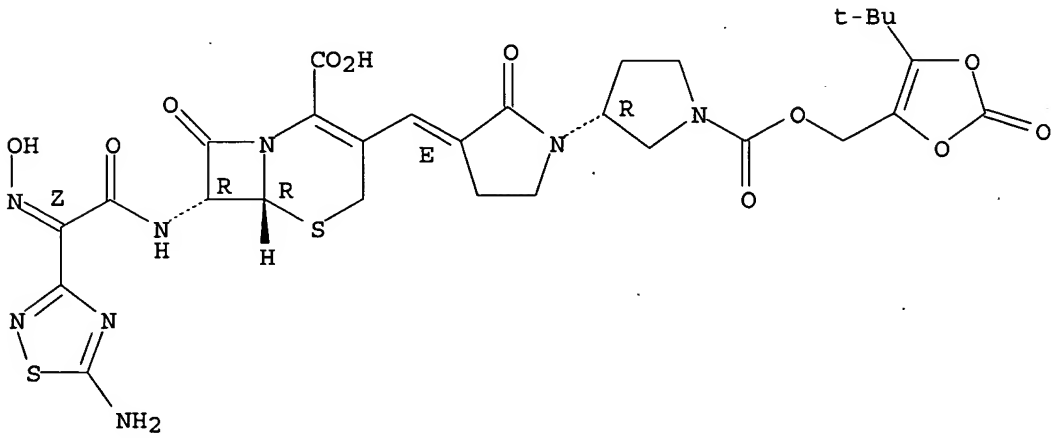
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-75-3 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-
[(3'R)-1'-[[[5-(1,1-dimethylethyl)-2-oxo-1,3-dioxol-4-yl]methoxy]carbonyl]-
2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt,
(6R,7R)- (9CI) (CA INDEX NAME)

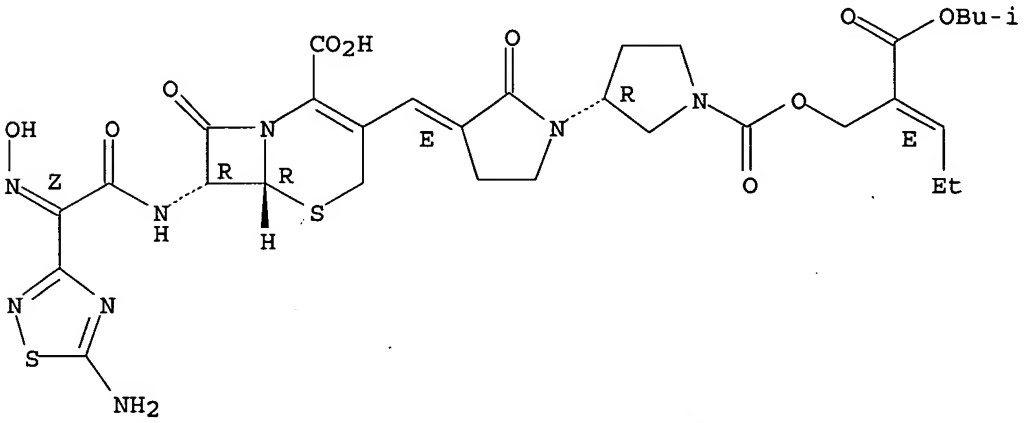
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-76-4 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[[[(2E)-2-[(2-methylpropoxy)carbonyl]-2-pentenyl]oxy]carbonyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)-(9CI) (CA INDEX NAME)

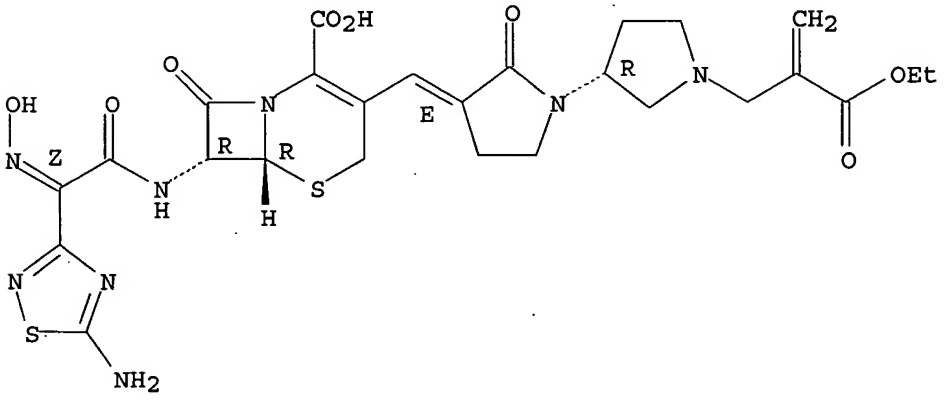
Absolute stereochemistry.
Double bond geometry as shown.



● Na

RN 252188-78-6 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-[2-(ethoxycarbonyl)-2-propenyl]-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

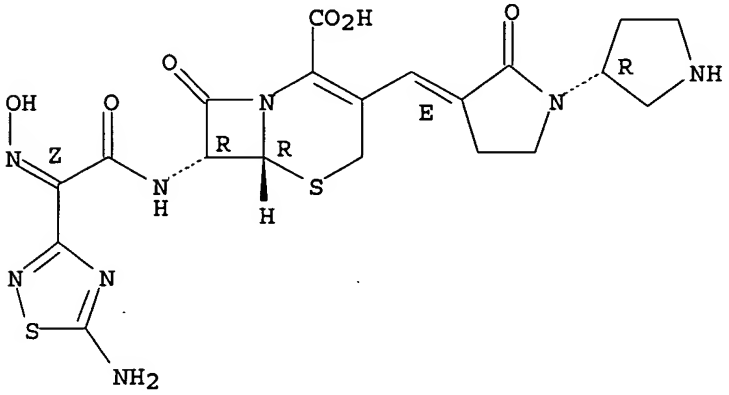
Absolute stereochemistry.
Double bond geometry as shown.



● Na

IT **209467-52-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and formulation of 3-(2-oxo-[1,3']bipyrrolidinyl-3-ylidenemethyl)-cephems for use as antibiotics)
RN 209467-52-7 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L28 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:424081 HCAPLUS
DN 129:81623
ED Entered STN: 10 Jul 1998
TI Preparation of vinylpyrrolidine derivatives of cephalosporins with basic substituents
IN Angehrn, Peter; Hebeisen, Paul; Heinze-Krauss, Ingrid; Page, Malcolm; Runtz, Valerie
PA F. Hoffmann-La Roche A.-G., Switz.
SO Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D501-34
ICS A61K031-545
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 849269	A1	19980624	EP 1997-121833	19971211 <--
	EP 849269	B1	20020710		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TW 415949	B	20001221	TW 1997-86118048	19971201 <--
	US 5981519	A	19991109	US 1997-986549	19971208 <--
	CA 2224438	AA	19980619	CA 1997-2224438	19971210 <--
	AT 220402	E	20020715	AT 1997-121833	19971211 <--
	PT 849269	T	20021129	PT 1997-121833	19971211 <--
	ES 2179996	T3	20030201	ES 1997-121833	19971211 <--

ZA 9711214	A	19980619	ZA 1997-11214	19971212	<--
NO 9705901	A	19980622	NO 1997-5901	19971216	<--
BR 9705650	A	19990525	BR 1997-5650	19971217	<--
AU 9748463	A1	19980625	AU 1997-48463	19971218	<--
AU 729653	B2	20010208			
CN 1188112	A	19980722	CN 1997-120875	19971218	<--
CN 1104436	B	20030402			
JP 10182657	A2	19980707	JP 1997-350413	19971219	<--
JP 3264877	B2	20020311			
JP 2002060390	A2	20020226	JP 2001-158260	19971219	<--
CN 1325850	A	20011212	CN 2000-133764	20001103	<--
CN 1347882	A	20020508	CN 2000-133761	20001103	<--
CN 1132833	B	20031231			
CN 1347883	A	20020508	CN 2000-133762	20001103	<--
CN 1347884	A	20020508	CN 2000-133763	20001103	<--
PRAI EP 1996-120472	A	19961219	<--		
EP 1997-119528	A	19971107	<--		
JP 1997-350413	A3	19971219	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 849269	ICM	C07D501-34
	ICS	A61K031-545
EP 849269	ECLA	C07D417/12+285B+277; C07D501/00; C07F009/572K4; C07F009/6558B <--
US 5981519	NCL	514/202.000; 514/203.000; 540/222.000; 540/225.000
	ECLA	C07D417/12+285B+277; C07D501/00; C07F009/572K4; C07F009/6558B <--

OS MARPAT 129:81623

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to cephalosporin derivs. I [X = CH or N; R1 = H, cyclopentyl; R2 = N-(R4)-azetidin-3-yl, R8, N-(R4),N'-(R4)-pyrazolidin-4-yl, (R)-N-(R4)-pyrrolidin-3-yl, (S)-N-(R4)-pyrrolidin-3-yl, (N-R4-azetidin-3-yl)methyl, R9, (N-R4,N'-R4-pyrazolidin-4-yl)methyl, (N-R4-piperidin-4-yl)methyl, 2-(4-R4-piperazin-1-yl)ethyl, (N-R4-pyrrolidin-2-yl)methyl, CH2C(NHR4):NH, CH2CH2NR4R7; R3 = H, alkali metal ion, tertiary ammonium group; R4 = H, amino protecting group, (pyrrolidin-2-yl)methyl, (azetidin-3-yl)methyl, iminomethyl, 1-carbamimidoyl; R5 = H, dialkylcarbamoyl, ω-hydroxyalkyl, ω-aminoalkyl, (pyridinium-1-yl)methyl, 1-hydroxy-3-aminomethyl-Pr or (hydroxy)(pyrrolidin-2-yl)methyl; R6 = H, trifluoromethyl or hydroxy; and R7 = alkyl, ω-hydroxy-alkyl, cycloalkyl, 3-pyrrolidinyl, 3-azetidinyl, iminomethyl, 1-carbamimidoyl] as well as readily hydrolyzable esters thereof, pharmaceutically acceptable salts of said compds. and hydrates of the aforementioned compds., to the manufacture of said compds.and to their use as pharmaceutically active substances, particularly for the treatment and prophylaxis of infectious diseases. Thus, II was prepared via N-acylation of the trifluoroacetate of cephem III with iminothioacetate IV followed by deprotection. II was active in vitro [MIC = 0.5 μg/mL vs. S. aureus 6538 (MSSA); MIC = 2 μg/mL vs. S. aureus 743 (MRSA); MIC = 2 μg/mL vs. S. aureus 270A (MRSA); MIC = 2 μg/mL vs. P. aeruginosa ATCC27853] and in vivo [median log CFU = 4.72 in mice infected with S. aureus 270A (MRSA)].

ST cephalosporin vinylpyrrolidine deriv prepn antibacterial

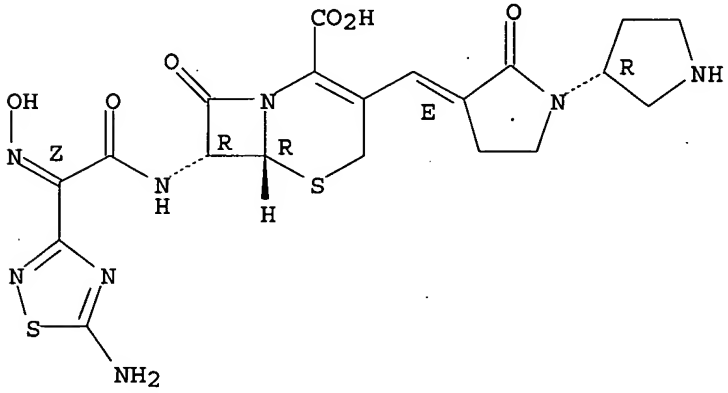
IT Antibacterial agents
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)
IT Lactams
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(β-, antibiotics; preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)
IT Lactams
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β-, antibiotics; preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)
IT 208179-72-0P **209467-52-7P** 209467-59-4P 209467-92-5P
209467-93-6P 209467-95-8P 209467-96-9P 209467-97-0P 209467-98-1P
209467-99-2P 209468-00-8P 209468-01-9P 209468-02-0P 209468-03-1P
209468-04-2P 209468-05-3P 209468-06-4P 209468-07-5P 209468-09-7P
209468-10-0P 209468-12-2P 209468-13-3P 209468-16-6P 209468-19-9P
209468-20-2P 209468-24-6P 209468-25-7P 209468-26-8P 209468-27-9P
209468-28-0P 209468-30-4P 209468-31-5P 209468-32-6P 209468-33-7P
209468-34-8P 209468-35-9P 209468-36-0P 209468-37-1P 209468-38-2P
209468-39-3P 209468-40-6P 209468-41-7P 209468-42-8P 209468-43-9P
209468-45-1P 209468-46-2P 209468-47-3P 209468-49-5P 209468-51-9P
209468-53-1P 209468-55-3P 209468-56-4P 209468-58-6P 209468-60-0P
209468-62-2P 209468-64-4P 209468-65-5P 209468-66-6P 209468-67-7P
209468-68-8P 209468-69-9P 209468-70-2P 209468-71-3P 209468-73-5P
209468-74-6P 209468-75-7P 209468-76-8P 209468-77-9P 209468-78-0P
209468-79-1P 209468-80-4P 209468-81-5P 209468-83-7P 209468-84-8P
209468-85-9P 209468-86-0P 209468-88-2P 209468-89-3P 209468-90-6P
209468-91-7P 209468-92-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)
IT 120-78-5 16694-46-5 19503-26-5 71254-32-5 124416-51-9
128438-02-8 175917-64-3 206994-45-8 209467-89-0 209467-91-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)
IT **209467-53-8P 209467-54-9P 209467-56-1P**
209467-57-2P 209467-58-3P **209467-60-7P 209467-61-8P**
209467-62-9P 209467-64-1P 209467-66-3P 209467-67-4P
209467-68-5P 209467-69-6P 209467-70-9P 209467-71-0P 209467-72-1P
209467-73-2P 209467-74-3P 209467-75-4P 209467-76-5P 209467-77-6P
209467-78-7P 209467-79-8P 209467-80-1P 209467-82-3P 209467-83-4P
209467-84-5P 209467-85-6P 209467-86-7P 209467-87-8P 209468-11-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Biochemie Gmbh; WO 9703990 A HCAPLUS
(2) Eisai Co Ltd; EP 0408034 A HCAPLUS
(3) Heinze-Krauss; J MED CHEM 1996, V39(9), P1864 HCAPLUS
(4) Hoffmann La Roche; EP 0620225 A HCAPLUS
(5) Kaisha, M; EP 0723965 A HCAPLUS
(6) Meiji Seika Co; EP 0774466 A HCAPLUS
(7) Terasawa, T; WO 9410177 A HCAPLUS

IT **209467-52-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)

RN 209467-52-7 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

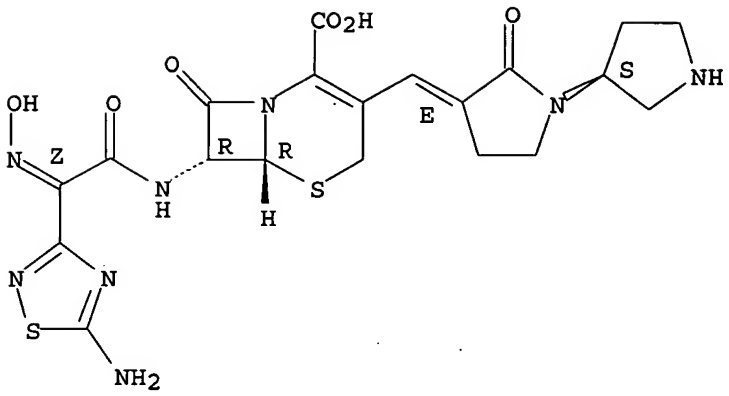
Absolute stereochemistry.
Double bond geometry as shown.



IT **209467-53-8P 209467-54-9P 209467-56-1P**
209467-60-7P 209467-61-8P 209467-62-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of vinylpyrrolidine derivs. of cephalosporins for treatment and prophylaxis of infectious diseases)

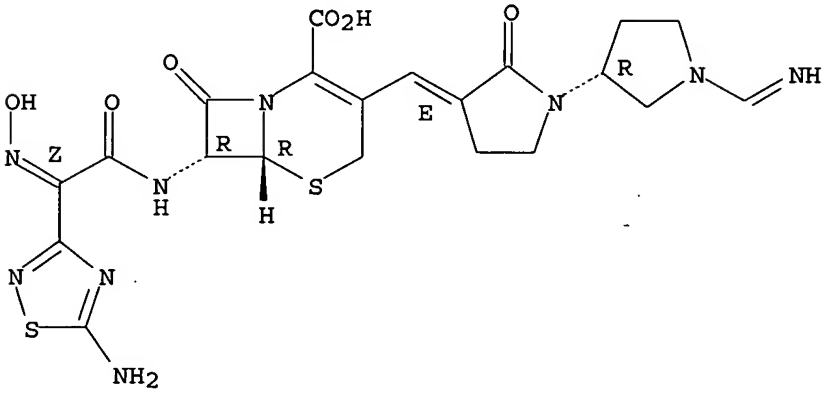
RN 209467-53-8 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'S)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



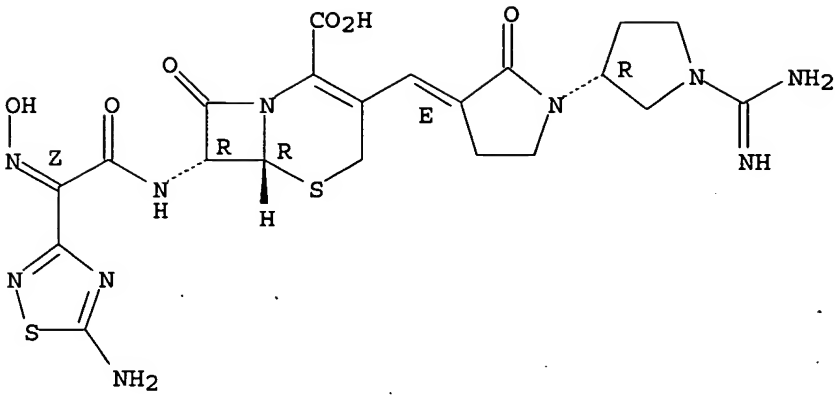
RN 209467-54-9 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-3-[(E)-[(3'R)-1'-(iminomethyl)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



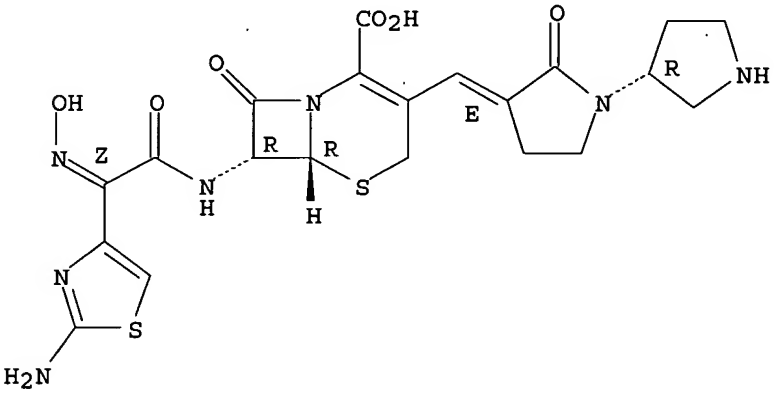
RN 209467-56-1 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(E)-[(3'R)-1'-(aminoiminomethyl)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-7-[[(2Z)-(5-amino-1,2,4-thiadiazol-3-yl)(hydroxyimino)acetyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



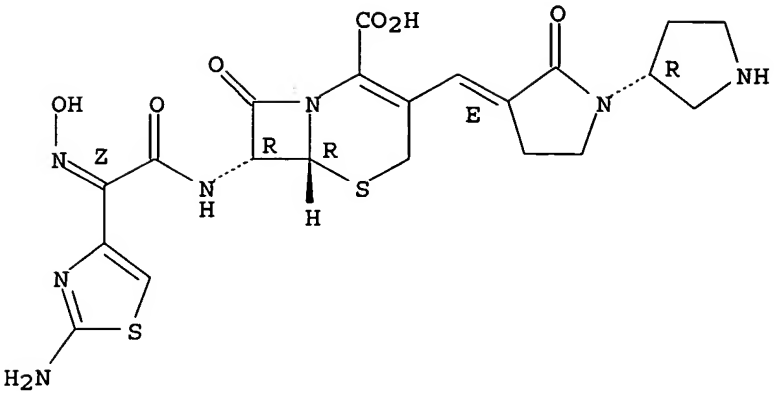
RN 209467-60-7 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209467-61-8 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'R)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, dihydrochloride, (6R,7R)- (9CI) (CA INDEX NAME)

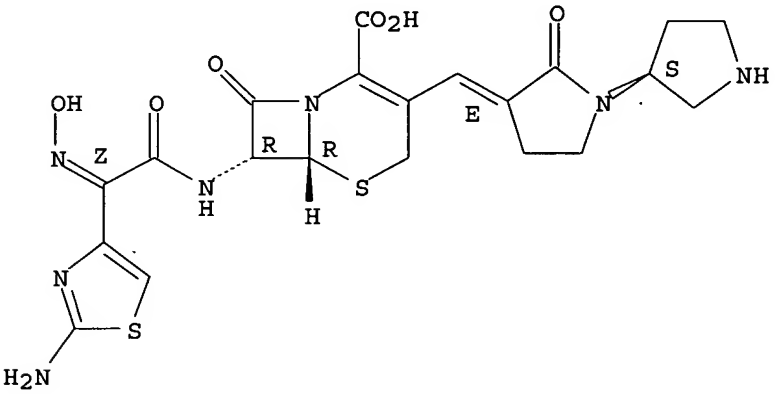
Absolute stereochemistry.
Double bond geometry as shown.



●2 HCl

RN 209467-62-9 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2Z)-(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-8-oxo-3-[(E)-[(3'S)-2-oxo[1,3'-bipyrrolidin]-3-ylidene]methyl]-, dihydrochloride, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



●2 HCl

=> d his

(FILE 'HOME' ENTERED AT 12:36:22 ON 04 AUG 2005)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 12:36:46 ON 04 AUG 2005
L1 STR
L2 0 S L1

```
L3            96 S L1 FUL
                 SAV L3 SHIAO743/A
L4               STR L1
L5             0 S L4 CSS SAM SUB=L3
L6            53 S L4 CSS FUL SUB=L3
                 SAV L6 SHIAO743A/A
L7               STR L4
L8            25 S L7 CSS FUL SUB=L6
                 SAV L8 SHIAO743B/A

     FILE 'HCAOLD' ENTERED AT 12:42:09 ON 04 AUG 2005
L9             0 S L8

     FILE 'HCAPLUS' ENTERED AT 12:42:40 ON 04 AUG 2005
L10           27 S L8

     FILE 'HCAPLUS' ENTERED AT 12:43:14 ON 04 AUG 2005
L11           22 S CEFTOBIPROLE OR BAL9141 OR BAL 9141 OR RO 63 9141 OR RO 65 57
L12           29 S L10,L11
L13            1 S (US20040127703 OR US6872836 OR US20040034236#)/PN OR (US2003-
                 E MULLER M/AU
L14          899 S E3-E27
                 E MULLER MARC/AU
L15           69 S E3-E5
                 E MUELLER MARC/AU
L16           28 S E3-E6
                 E MUELLER M/AU
L17         1295 S E3-E25
                 E MEULLER M/AU
L18            1 S E5
                 E SOUKUP M/AU
L19           36 S E3,E9
                 E BASO
                 E BASILEA/PA,CS
L20           41 S E3-E17
L21            5 S L12 AND L13-L20
L22           29 S L12 OR BAL5788
L23            5 S L22 AND L13-L20
L24           15 S L22 AND (PY<=2002 OR PRY<=2002 OR AY<=2002)
L25            6 S L22 (L) PREP+NT/RL
L26            5 S L24 AND L25
L27            8 S L23,L26
L28            8 S L25-L27
L29           10 S L24 NOT L28

     FILE 'USPATFULL' ENTERED AT 12:51:59 ON 04 AUG 2005
L30            5 S L8/P

     FILE 'REGISTRY' ENTERED AT 12:52:28 ON 04 AUG 2005

     FILE 'USPATFULL' ENTERED AT 12:52:39 ON 04 AUG 2005

     FILE 'HCAPLUS' ENTERED AT 12:52:48 ON 04 AUG 2005

=>
```